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(54) Title: BORRELIA BURGDORFERI POLYNUCLEOTIDES AND SEQUENCES

(57) Abstract

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The present invention provides polynucleotide sequences of the genome of Borrelia Burgdorferi, polypeptide sequences encoded by the polynucleotide sequences, corresponding polynucleotides and polypeptides, vectors and hosts comprising the polynucleotides, and assays and other uses thereof. The present invention further provides polynucleotide and polypeptide sequence information stored on computer readable media, and computer-based systems and methods which facilitate its use.

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Borrelia burgdorferi Polynucleotides and Sequences

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Field of the Invention

The present invention relates to the field of molecular biology. In particular, it relates to, among other things, nucleotide sequences of *Borrelia burgdorferi*, contigs, ORFs, fragments, probes, primers and related polynucleotides thereof, peptides and polypeptides encoded by the sequences, and uses of the polynucleotides and sequences thereof, such as in fermentation, polypeptide production, assays and pharmaceutical development, among others.

Statement as to Rights to Inventions Made Under Federally-Sponsored Research and Development

Part of the work performed during development of this invention utilized U.S. Government funds. The U.S. Government may have certain rights in the invention - DE-FC02-95ER61962; DE-FC02-95ER61963; and NAGW 2554.

Background of the Invention

Spirochetes are a family of motile, unicellular, spiral-shaped bacteria which share a number of structural characteristics. Three genera of the spirochetes are pathogenic in humans: (a) *Treponema*, which includes the pathogens that cause syphilis (*T. pallidum*), yaws (*T. pertenue*), and pinta (*T. carateum*); (b) *Borrelia*, which includes the pathogens that cause epidemic and endemic relapsing fever and Lyme disease; and (c) *Leptospira*, which includes a wide variety of small spirochetes that cause mild to serious systemic human illness (Koff, A. B. and Rosen, T. *J. Am. Acad. Dermatol.* **29:**519-535 (1993)).

Lyme borreliosis, more commonly known as Lyme disease, is presently the most common human disease in the United States transmitted by an arthropod vector. Centers for Disease Control, Morbid. Mortal. Weekly Rep. 44:590-591 (1995). Further, infection of household pets, such as dogs, is a considerable problem. The causative agent of this affliction is the spirochete *Borrelia burgdorferi*, which is generally transmitted to mammalian hosts by feeding ticks. Barbour, A. and Fish, D. Science 260:1610-1616 (1993). Once the bacteria pass through the skin they disseminate and produce a variety of clinical manifestations. Diagnosis of this disease is often made serologically by the identification of antiborrelial antibodies. Hilton, E. et al., J. Clin. Microbiol. 35:774-776 (1997).

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While initial symptoms often include a rash at the infection point, Lyme disease is a multisystemic disorder that may include arthritic, carditic, and neurological manifestations. While antibiotics are currently used to treat active cases of Lyme disease, *B. burgdorferi* appears to be able to persist even after prolonged antibiotic treatment. Further, *B. burgdorferi* can persist for years in a mammalian host even in the presence of an active immune response. Straubinger, R. et al., J. Clin. Microbiol. 35:111-116 (1997); Steere, A., N. Engl. J. Med. 321:586-596 (1989).

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Animal models have proven useful for studying the progression of Lyme disease, methods for preventing this disease, and immunological responses to antigenic challenges with *B. burgdorferi* proteins. Garcia-Monoco, J. et al., J. Infect. Dis. 175:1243-1245 (1997). Using a canine model, Starubinger, R. et al., Infect. Immun. 65:1273-1285 (1977), demonstrated that *B. burgdorferi* migrates into joints and induces up-regulation of interleukin-8 in synovial membranes. Similarly, *B. burgdorferi* induction of interleukin-8 production has been demonstrated in cultured human endothelial cells. Burns, M. et al., Infect. Immun. 65:1217-1222 (1997).

Antigenic heterogeneity has been postulated as a mechanism used by *B. burgdorferi* for evasion of host immune responses. Schwan, T. et al., Can. J. Microbiol. 37:450-454 (1991). In support of this mechanism, antigenic variation has been described with other pathogenic bacteria. Hagbloom, P. et al., Nature 315:156-158 (1985). Further, cassette type genetic recombination of genes encoding *B. burgdorferi* surface proteins has been shown to decrease the antigenicity of these organisms to antibodies generated against strains which have not undone the same recombination. Zhang, J. et al., Cell 89:275-285 (1997).

A number of different types of Lyme disease vaccines have been tested and shown to induce immunological responses. Whole-cell *B. burgdorferi* vaccines have been shown to induce both immunological responses and protective immunity in several animal models. Reviewed in Wormser, G., Clin. Infect. Dis. 21:1267-1274 (1995). For example, dogs inoculated with a chemically inactivated whole-cell vaccine primarily develop antibodies to outer surface membrane proteins of the administered organism. Further, passive immunity has been also demonstrated in animals using *B. burgdorferi* specific antisera. Similarly, passive immunity is conferred human by the administration of sera obtained from Lyme disease patients.

While whole-cell Lyme disease vaccines confer protective immunity in animal models, use of such vaccines presents the risk that responsive antibodies will be generated which cross react with human antigens. Reviewed in Wormser, G., supra. This problem is at least partly the result of the production of *B. burgdorferi* specific antibodies which cross-react with hepatocytes and both muscle and nerve cells. *B. burgdorferi* heat shock proteins and the 41-kd flagellin subunit are believed to contain the antigens against which these cross-reactive antibodies are generated.

It is clear that the etiology of diseases mediated or exacerbated by *B. burgdorferi* genes, and that characterizing the genes and their patterns of expression would add dramatically to our

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understanding of the organism and its host interactions. Knowledge of *B. burgdorferi* genes and genomic organization would dramatically improve understanding of disease etiology and lead to improved and new ways of preventing, ameliorating, arresting and reversing diseases. Moreover, characterized genes and genomic fragments of *B. burgdorferi* would provide reagents for, among other things, detecting, characterizing and controlling *B. burgdorferi* infections. There is a need therefore to characterize the genome of *B. burgdorferi* and for polynucleotides and sequences of this organism.

SUMMARY OF THE INVENTION

The present invention is based on the sequencing of fragments of the *Borrelia burgdorferi* genome. The primary nucleotide sequences which were generated are provided in SEQ ID NOS:1-155.

The present invention provides the complete nucleotide sequence of the *Borrelia burgdorferi* chromosome and 154 contigs representing the majority of the sequence of the B. burgdorferi extrachromosomal elements, all of which are listed in tables below and set out in the Sequence Listing submitted herewith, and representative fragments thereof, in a form which can be readily used, analyzed, and interpreted by a skilled artisan. In one embodiment, the present invention is provided as contiguous strings of primary sequence information corresponding to the nucleotide sequences depicted in SEQ ID NOS: 1-155.

The present invention further provides nucleotide sequences which are at least 95%, 96%, 97%, 98%, and 99%, identical to the nucleotide sequences of SEQ ID NOS:1-155, ORF IDs and corresponding ORFs.

The nucleotide sequences of SEQ ID NOS:1-155, ORF ID or ORF within, a representative fragment thereof, or a nucleotide sequence which is at least 95% identical to said nucleotide sequence may be provided in a variety of mediums to facilitate its use. In one application of this embodiment, the sequences of the present invention are recorded on computer readable media. Such media includes, but is not limited to: magnetic storage media, such as floppy discs, hard disc storage medium, and magnetic tape; optical storage media such as CD-ROM; electrical storage media such as RAM and ROM; and hybrids of these categories such as magnetic/optical storage media.

The present invention further provides systems, particularly computer-based systems which contain the sequence information herein described stored in a data storage means. Such systems are designed to identify commercially important fragments of the *Borrelia burgdorferi* genome.

Another embodiment of the present invention is directed to fragments of the *Borrelia* burgdorferi genome having particular structural or functional attributes. Such fragments of the *Borrelia burgdorferi* genome of the present invention include, but are not limited to, fragments which encode peptides, hereinafter referred to as open reading frames or ORFs, fragments which modulate the expression of an operably linked ORF, hereinafter referred to as expression

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modulating fragments or EMFs, and fragments which can be used to diagnose the presence of *Borrelia burgdorferi* in a sample, hereinafter referred to as diagnostic fragments or DFs.

Each of the ORF IDs and ORFs in fragments of the *Borrelia burgdorferi* genome disclosed in Tables 1-6, and the EMFs found 5' prime of the initiation codon, can be used in numerous ways as polynucleotide reagents. For instance, the sequences can be used as diagnostic probes or amplification primers for detecting or determining the presence of a specific microbe in a sample, to selectively control gene expression in a host and in the production of polypeptides, such as polypeptides encoded by ORFs of the present invention, particular those polypeptides that have a pharmacological activity.

The present invention further includes recombinant constructs comprising one or more fragments of the *Borrelia burgdorferi* genome of the present invention. The recombinant constructs of the present invention comprise vectors, such as a plasmid or viral vector, into which a fragment of the *Borrelia burgdorferi* has been inserted.

The present invention further provides host cells containing any of the isolated fragments of the *Borrelia burgdorferi* genome of the present invention. The host cells can be a higher eukaryotic host cell, such as a mammalian cell, a lower eukaryotic cell, such as a yeast cell, or a procaryotic cell such as a bacterial cell.

The present invention is further directed to isolated polypeptides and proteins encoded by ORFs of the present invention. A variety of methods, well known to those of skill in the art, routinely may be utilized to obtain any of the polypeptides and proteins of the present invention. For instance, polypeptides and proteins of the present invention having relatively short, simple amino acid sequences readily can be synthesized using commercially available automated peptide synthesizers. Polypeptides and proteins of the present invention also may be purified from bacterial cells which naturally produce the protein. Yet another alternative is to purify polypeptide and proteins of the present invention from cells which have been altered to express them.

The invention further provides methods of obtaining homologs of the fragments of the *Borrelia burgdorferi* genome of the present invention and homologs of the proteins encoded by the ORFs of the present invention. Specifically, by using the nucleotide and amino acid sequences disclosed herein as a probe or as primers, and techniques such as PCR cloning and colony/plaque hybridization, one skilled in the art can obtain homologs.

The invention further provides antibodies which selectively bind polypeptides and proteins of the present invention. Such antibodies include both monoclonal and polyclonal antibodies.

The invention further provides hybridomas which produce the above-described antibodies. A hybridoma is an immortalized cell line which is capable of secreting a specific monoclonal antibody.

The present invention further provides methods of identifying test samples derived from cells which express one of the ORFs of the present invention, or a homolog thereof. Such

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methods comprise incubating a test sample with one or more of the antibodies of the present invention, or one or more of the DFs of the present invention, under conditions which allow a skilled artisan to determine if the sample contains the ORF or product produced therefrom.

In another embodiment of the present invention, kits are provided which contain the necessary reagents to carry out the above-described assays.

Specifically, the invention provides a compartmentalized kit to receive, in close confinement, one or more containers which comprises: (a) a first container comprising one of the antibodies, or one of the DFs of the present invention; and (b) one or more other containers comprising one or more of the following: wash reagents, reagents capable of detecting presence of bound antibodies or hybridized DFs.

Using the isolated proteins of the present invention, the present invention further provides methods of obtaining and identifying agents capable of binding to a polypeptide or protein encoded by one of the ORFs of the present invention. Specifically, such agents include, as further described below, antibodies, peptides, carbohydrates, pharmaceutical agents and the like. Such methods comprise steps of: (a)contacting an agent with an isolated protein encoded by one of the ORFs of the present invention; and (b)determining whether the agent binds to said protein.

The present genomic sequences of *Borrelia burgdorferi* will be of great value to all laboratories working with this organism and for a variety of commercial purposes. Many fragments of the *Borrelia burgdorferi* genome will be immediately identified by similarity searches against GenBank or protein databases and will be of immediate value to *Borrelia burgdorferi* researchers and for immediate commercial value for the production of proteins or to control gene expression.

The methodology and technology for elucidating extensive genomic sequences of bacterial and other genomes has and will greatly enhance the ability to analyze and understand chromosomal organization. In particular, sequenced contigs and genomes will provide the models for developing tools for the analysis of chromosome structure and function, including the ability to identify genes within large segments of genomic DNA, the structure, position, and spacing of regulatory elements, the identification of genes with potential industrial applications, and the ability to do comparative genomic and molecular phylogeny.

DESCRIPTION OF THE FIGURES

FIGURE 1 is a block diagram of a computer system (102) that can be used to implement computer-based systems of present invention.

FIGURE 2 is a schematic diagram depicting the data flow and computer programs used to collect, assemble, edit and annotate the contigs of the *Borrelia burgdorferi* genome of the present invention. Both Macintosh and Unix platforms are used to handle the AB 373 and 377 sequence data files, largely as described in Kerlavage *et al.*, *Proceedings of the Twenty-Sixth*

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Annual Hawaii International Conference on System Sciences, 585, IEEE Computer Society Press, Washington D.C. (1993). Factura (AB) is a Macintosh program designed for automatic vector sequence removal and end-trimming of sequence files. The program Loadis runs on a Macintosh platform and parses the feature data extracted from the sequence files by Factura to the Unix based Borrelia burgdorferi relational database. Assembly of contigs (and whole genome sequences) is accomplished by retrieving a specific set of sequence files and their associated features using Extrseq, a Unix utility for retrieving sequences from an SQL database. The resulting sequence file is processed to trim portions of the sequences with a high rate ambiguous nucleotides. The sequence files were assembled using TIGR Assembler, an assembly engine designed at The Institute for Genomic Research (TIGR) for rapid and accurate assembly of thousands of sequence fragments. The collection of contigs generated by the assembly step is loaded into the database with the lassie program. Identification of open reading frames (ORFs) is accomplished by processing contigs with zorf. The ORFs are searched against B. burgdorferi sequences from GenBank and against all protein sequences using the BLASTN and BLASTP programs, described in Altschul et al., J. Mol. Biol. 215: 403-410 (1990). Results of the ORF determination and similarity searching steps were loaded into the database. As described below, some results of the determination and the searches are set out in Tables 1-6.

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

The present invention is based on the sequencing of fragments of the *Borrelia burgdorferi* genome and analysis of the sequences. The primary nucleotide sequences generated by sequencing the fragments are provided in SEQ ID NOS: 1-155. (As used herein, the "primary sequence" refers to the nucleotide sequence represented by the IUPAC nomenclature system.) SEQ ID NOS:1-155

In addition, the present invention provides the nucleotide sequences of SEQ ID NOS: 1-155, or representative fragments thereof, in a form which can be readily used, analyzed, and interpreted by a skilled artisan.

As used herein, a "representative fragment of the nucleotide sequence depicted in SEQ ID NOS:1-155" refers to any portion of the SEQ ID NOS: 1-155 which is not presently represented within a publicly available database. Preferred representative fragments of the present invention are *Borrelia burgdorferi* open reading frames (ORFs) represented by ORF IDs, expression modulating fragments (EMFs) and diagnostic fragments (DFs)which can be used to diagnose the presence of *Borrelia burgdorferi* in sample. A non-limiting identification of preferred representative portions are provided in Tables 1-6 as ORF IDs. As discussed in detail below, the information provided in SEQ ID NOS:1-155 and in Tables 1-6 together with routine cloning, synthesis, sequencing and assay methods will enable those skilled in the art to clone and sequence all "representative fragments" of interest, including ORFs encoding a large variety of *Borrelia burgdorferi* proteins.

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The present invention is further directed to nucleic acid molecules encoding portions or fragments of the nucleotide sequences described herein. Fragments include portions of the nucleotide sequences of Table 1-6 (ORF IDs) and SEQ ID NOS:1-155, at least 10 contiguous nucleotides in length selected from any two integers, one of which representing a 5' nucleotide position and a second of which representing a 3' nucleotide position, where the first nucleotide for each nucleotide sequence in SEQ ID NOS:1-155 is position 1 (therefore, the sequence postions for each ORF ID is determined by the numbering of the SEQ ID comprising the ORF ID). That is, every combination of a 5' and 3' nucleotide position that a fragment at least 10 contiguous nucleotides in length could occupy is included in the invention. At least means a fragment may be 10 contiguous nucleotide bases in length or any integer between 10 and the length of an entire nucleotide sequence of SEQ ID NOS:1-155 minus 1. Therefore, included in the invention are contiguous fragments specified by any 5' and 3' nucleotide base positions of a nucleotide sequences of SEQ ID NOS:1-155 wherein the contiguous fragment is any integer between 10 and the length of an entire nucleotide sequence minus 1.

Further, the invention includes polynucleotides comprising fragments specified by size, in nucleotides, rather than by nucleotide positions. The invention includes any fragment size, in contiguous nucleotides, selected from integers between 10 and the length of an entire ORF ID or SEQ ID NO:, minus 1. Preferred sizes of contiguous nucleotide fragments include 20 nucleotides, 30 nucleotides, 40 nucleotides, 50 nucleotides. Other preferred sizes of contiguous nucleotide fragments, which may be useful as diagnostic probes and primers, include fragments 50-300 nucleotides in length which include, as discussed above, fragment sizes representing each integer between 50-300. Larger fragments are also useful according to the present invention corresponding to most, if not all, of the nucleotide sequences shown in Tables 1-6 (ORF IDs) and SEQ ID NOS:1-155. The preferred sizes are, of course, meant to exemplify not limit the present invention as all size fragments, representing any integer between 10 and the length of an entire nucleotide sequence minus 1, of each ORF ID and SEQ ID NO:, are included in the invention.

The present invention also provides for the exclusion of any fragment, specified by 5' and 3' base positions or by size in nucleotide bases as described above for any ORF ID or SEQ ID NOS:1-155. Any number of fragments of nucleotide sequences in ORF IDs or SEQ ID NOS:1-155, specified by 5' and 3' base positions or by size in nucleotides, as described above, may be excluded from the present invention.

While the presently disclosed sequences of SEQ ID NOS: 1-155 are highly accurate, sequencing techniques are not perfect and, in relatively rare instances, further investigation of a fragment or sequence of the invention may reveal a nucleotide sequence error present in a nucleotide sequence disclosed in SEQ ID NOS: 1-155. However, once the present invention is made available (*i.e.*, once the information in SEQ ID NOS: 1-155 and Tables 1-6 has been made available), resolving a rare sequencing error in SEQ ID NOS: 1-155 will be well within the skill

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of the art. The present disclosure makes available sufficient sequence information to allow any of the described contigs or portions thereof to be obtained readily by straightforward application of routine techniques. Further sequencing of such polynucleotide may proceed in like manner using manual and automated sequencing methods which are employed ubiquitous in the art. Nucleotide sequence editing software is publicly available. For example, Applied Biosystem's (AB) AutoAssembler can be used as an aid during visual inspection of nucleotide sequences. By employing such routine techniques potential errors readily may be identified and the correct sequence then may be ascertained by targeting further sequencing effort, also of a routine nature, to the region containing the potential error.

Even if all of the very rare sequencing errors in SEQ ID NOS: 1-155 were corrected, the resulting nucleotide sequences would still be at least 95% identical, nearly all would be at least 99% identical, and the great majority would be at least 99.9% identical to the nucleotide sequences of SEQ ID NOS: 1-155.

As discussed elsewhere herein, polynucleotides of the present invention readily may be obtained by routine application of well known and standard procedures for cloning and sequencing DNA. Detailed methods for obtaining libraries and for sequencing are provided below, for instance. A wide variety of *Borrelia burgdorferi* strains that can be used to prepare *B. burgdorferi* genomic DNA for cloning and for obtaining polynucleotides of the present invention are available to the public from recognized depository institutions, such as the American Type Culture Collection (ATCC). While the present invention is enabled by the sequences and other information herein disclosed, the *B. burgdorferi* strain that provided the DNA of the present Sequence Listing, has been deposited with the ATCC, 10801 University Blvd. Manassas, VA 20110-2209, as Deposit No. 202012, on 8 August 1997. The ATCC Deposit is provided merely as a convenience to those of skill in the art. Reference to the deposit is not a waiver of any rights of the inventors or their assignees in the present subject matter.

The nucleotide sequences of the genomes from different strains of *Borrelia burgdorferi* differ somewhat. However, the nucleotide sequences of the genomes of all *Borrelia burgdorferi* strains will be at least 95% identical, in corresponding part, to the nucleotide sequences provided in SEQ ID NOS: 1-155 and the ORF IDs within. Nearly all will be at least 99% identical and the great majority will be 99.9% identical.

The present application is further directed to nucleic acid molecules at least 90%, 95%, 96%, 97%, 98% or 99% identical to a nucleic acid sequence shown in SEQ ID NOS: 1-155 and the ORF IDs within. The above nucleic acid sequences are included irrespective of whether they encode a polypeptide having *B. burgdorferi* activity. This is because even where a particular nucleic acid molecule does not encode a polypeptide having *B. burgdorferi* activity, one of skill in the art would still know how to use the nucleic acid molecule, for instance, as a hybridization probe. Uses of the nucleic acid molecules of the present invention that do not encode a polypeptide having *B. burgdorferi* activity include, *inter alia*, isolating a *B. burgdorferi* gene or allelic variants thereof from a DNA library, and detecting *B. burgdorferi* mRNA expression from

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biological or environmental samples, suspected of containing *B. burgdorferi* by Northern Blot, PCR, or similar analysis.

Preferred, are nucleic acid molecules having sequences at least 90%, 95%, 96%, 97%, 98% or 99% identical to the nucleic acid sequence shown in SEQ ID NOS: 1-155, the ORF IDs, and the ORF within each ORF ID, which do, in fact, encode a polypeptide having *B. burgdorferi* protein activity. By "a polypeptide having *B. burgdorferi* activity" is intended polypeptides exhibiting activity similar, but not necessarily identical, to an activity of the *B. burgdorferi* protein of the invention, as measured in a particular biological assay suitable for measuring activity of the specified protein.

Due to the degeneracy of the genetic code, one of ordinary skill in the art will immediately recognize that a large number of the nucleic acid molecules having a sequence at least 90%, 95%, 96%, 97%, 98%, or 99% identical to the nucleic acid sequences shown in SEQ ID NOS: 1-155, the ORF IDs, and the ORF within each ORF ID, will encode a polypeptide having *B. burgdorferi* protein activity. In fact, since degenerate variants of these nucleotide sequences all encode the same polypeptide, this will be clear to the skilled artisan even without performing the above described comparison assay. It will be further recognized in the art that, for such nucleic acid molecules that are not degenerate variants, a reasonable number will also encode a polypeptide having *B. burgdorferi* protein activity. This is because the skilled artisan is fully aware of amino acid substitutions that are either less likely or not likely to significantly effect protein function (e.g., replacing one aliphatic amino acid with a second aliphatic amino acid), as further described below.

The biological activity or function of the polypeptides of the present invention are expected to be similar or identical to polypeptides from other bacteria that share a high degree of structural identity/similarity. Tables 1, 2, 4, and 5 lists accession numbers and descriptions for the closest matching sequences of polypeptides available through Genbank. It is therefore expected that the biological activity or function of the polypeptides of the present invention will be similar or identical to those polypeptides from other bacterial genuses, species, or strains listed in Tables 1, 2, 4, and 5.

By a polynucleotide having a nucleotide sequence at least, for example, 95% "identical" to a reference nucleotide sequence of the present invention, it is intended that the nucleotide sequence of the polynucleotide is identical to the reference sequence except that the polynucleotide sequence may include up to five point mutations per each 100 nucleotides of the reference nucleotide sequence encoding the *B. burgdorferi* polypeptide. In other words, to obtain a polynucleotide having a nucleotide sequence at least 95% identical to a reference nucleotide sequence, up to 5% of the nucleotides in the reference sequence may be deleted, inserted, or substituted with another nucleotide. The query sequence may be an entire sequence shown in SEQ ID NOS: 1-155, an ORF ID, or the ORF within each ORF ID, or any fragment specified as described herein.

As a practical matter, whether any particular nucleic acid molecule or polypeptide is at least 90%, 95%, 96%, 97%, 98% or 99% identical to a nucleotide sequence of the presence invention can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. *See* Brutlag et al. (1990) Comp. App. Biosci. 6:237-245. In a sequence alignment the query and subject sequences are both DNA sequences. An RNA sequence can be compared by first converting U's to T's. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB alignment of DNA sequences to calculate percent identity are: Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining Penalty=30, Randomization Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty=0.05, Window Size=500 or the length of the subject nucleotide sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence because of 5' or 3' deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for 5' and 3' truncations of the subject sequence when calculating percent identity. For subject sequences truncated at the 5' or 3' ends, relative to the query sequence, the percent identity is corrected by calculating the number of bases of the query sequence that are 5' and 3' of the subject sequence, which are not matched/aligned, as a percent of the total bases of the query sequence. Whether a nucleotide is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This corrected score is what is used for the purposes of the present invention. Only nucleotides outside the 5' and 3' nucleotides of the subject sequence, as displayed by the FASTDB alignment, which are not matched/aligned with the query sequence, are calculated for the purposes of manually adjusting the percent identity score.

For example, a 90 nucleotide subject sequence is aligned to a 100 nucleotide query sequence to determine percent identity. The deletions occur at the 5' end of the subject sequence and therefore, the FASTDB alignment does not show a matched/alignment of the first 10 nucleotides at 5' end. The 10 unpaired nucleotides represent 10% of the sequence (number of nucleotides at the 5' and 3' ends not matched/total number of nucleotides in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 nucleotides were perfectly matched the final percent identity would be 90%. In another example, a 90 nucleotide subject sequence is compared with a 100 nucleotide query sequence. This time the deletions are internal deletions so that there are no nucleotides on the 5' or 3' of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only nucleotides 5' and 3' of the

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subject sequence which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to made for the purposes of the present invention.

COMPUTER RELATED EMBODIMENTS

The nucleotide sequences provided in SEQ ID NOS: 1-155, including ORF IDs and corresponding ORFs, a representative fragment thereof, or a nucleotide sequence at least 95%, preferably at least 96%, 97%, 98% or 99%, and most preferably at least 99.9% identical to said nucleotide sequences may be "provided" in a variety of mediums to facilitate use thereof. As used herein, provided refers to a manufacture, other than an isolated nucleic acid molecule; which contains a nucleotide sequence of the present invention, a representative fragment thereof, or a nucleotide sequence at least 95%, preferably at least 99% and most preferably at least 99.9% identical to a polynucleotide of the present invention. Such a manufacture provides a large portion of the *Borrelia burgdorferi* genome and parts thereof (*e.g.*, a *Borrelia burgdorferi* open reading frame (ORF)) in a form which allows a skilled artisan to examine the manufacture using means not directly applicable to examining the *Borrelia burgdorferi* genome or a subset thereof as it exists in nature or in purified form.

In one application of this embodiment, a nucleotide sequence of the present invention can be recorded on computer readable media. As used herein, "computer readable media" refers to any medium which can be read and accessed directly by a computer. Such media include, but are not limited to: magnetic storage media, such as floppy discs, hard disc storage medium, and magnetic tape; optical storage media such as CD- ROM; electrical storage media such as RAM and ROM; and hybrids of these categories, such as magnetic/optical storage media. A skilled artisan can readily appreciate how any of the presently known computer readable mediums can be used to create a manufacture comprising computer readable medium having recorded thereon a nucleotide sequence of the present invention. Likewise, it will be clear to those of skill how additional computer readable media that may be developed also can be used to create analogous manufactures having recorded thereon a nucleotide sequence of the present invention.

As used herein, "recorded" refers to a process for storing information on computer readable medium. A skilled artisan can readily adopt any of the presently know methods for recording information on computer readable medium to generate manufactures comprising the nucleotide sequence information of the present invention.

A variety of data storage structures are available to a skilled artisan for creating a computer readable medium having recorded thereon a nucleotide sequence of the present invention. The choice of the data storage structure will generally be based on the means chosen to access the stored information. In addition, a variety of data processor programs and formats can be used to store the nucleotide sequence information of the present invention on computer readable medium. The sequence information can be represented in a word processing text file, formatted in commercially- available software such as WordPerfect and MicroSoft Word, or represented in the form of an ASCII file, stored in a database application, such as DB2, Sybase,

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Oracle, or the like. A skilled artisan can readily adapt any number of data-processor structuring formats (e.g., text file or database) in order to obtain computer readable medium having recorded thereon the nucleotide sequence information of the present invention.

Computer software is publicly available which allows a skilled artisan to access sequence information provided in a computer readable medium. Thus, by providing in computer readable form the nucleotide sequences of the present invention (e.g. SEQ ID NOS: 1-155), a representative fragment thereof, or a nucleotide sequence at least 95%, preferably at least 96%, 97%, 98%, 99% and most preferably at least 99.9% identical to a sequence of the present invention (e.g. SEQ ID NOS: 1-155) enables the skilled artisan routinely to access the provided sequence information for a wide variety of purposes.

The examples which follow demonstrate how software which implements the BLAST (Altschul et al., J. Mol. Biol. 215:403-410 (1990)) and BLAZE (Brutlag et al., Comp. Chem. 17:203-207 (1993)) search algorithms on a Sybase system was used to identify open reading frames (ORFs) within the Borrelia burgdorferi genome which contain homology to ORFs or proteins from both Borrelia burgdorferi and from other organisms. Among the ORFs discussed herein are protein encoding fragments of the Borrelia burgdorferi genome useful in producing commercially important proteins, such as enzymes used in fermentation reactions and in the production of commercially useful metabolites.

The present invention further provides systems, particularly computer-based systems, which contain the sequence information described herein. Such systems are designed to identify, among other things, commercially important fragments of the *Borrelia burgdorferi* genome.

As used herein, "a computer-based system" refers to the hardware means, software means, and data storage means used to analyze the nucleotide sequence information of the present invention. The minimum hardware means of the computer-based systems of the present invention comprises a central processing unit (CPU), input means, output means, and data storage means. A skilled artisan can readily appreciate that any one of the currently available computer-based system are suitable for use in the present invention.

As stated above, the computer-based systems of the present invention comprise a data storage means having stored therein a nucleotide sequence of the present invention and the necessary hardware means and software means for supporting and implementing a search means.

As used herein, "data storage means" refers to memory which can store nucleotide sequence information of the present invention, or a memory access means which can access manufactures having recorded thereon the nucleotide sequence information of the present invention.

As used herein, "search means" refers to one or more programs which are implemented on the computer-based system to compare a target sequence or target structural motif with the sequence information stored within the data storage means. Search means are used to identify fragments or regions of the present genomic sequences which match a particular target sequence or target motif. A variety of known algorithms are disclosed publicly and a variety of

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commercially available software for conducting search means are and can be used in the computer-based systems of the present invention. Examples of such software includes, but is not limited to, MacPattern (EMBL), BLASTN and BLASTX (NCBIA). A skilled artisan can readily recognize that any one of the available algorithms or implementing software packages for conducting homology searches can be adapted for use in the present computer-based systems.

As used herein, a "target sequence" can be any DNA or amino acid sequence of six or more nucleotides or two or more amino acids. A skilled artisan can readily recognize that the longer a target sequence is, the less likely a target sequence will be present as a random occurrence in the database. The most preferred sequence length of a target sequence is from about 10 to 100 amino acids or from about 30 to 300 nucleotide residues. However, it is well recognized that searches for commercially important fragments, such as sequence fragments involved in gene expression and protein processing, may be of shorter length.

As used herein, "a target structural motif," or "target motif," refers to any rationally selected sequence or combination of sequences in which the sequence(s) are chosen based on a three-dimensional configuration which is formed upon the folding of the target motif. There are a variety of target motifs known in the art. Protein target motifs include, but are not limited to, enzymic active sites and signal sequences. Nucleic acid target motifs include, but are not limited to, promoter sequences, hairpin structures and inducible expression elements (protein binding sequences).

A variety of structural formats for the input and output means can be used to input and output the information in the computer-based systems of the present invention. A preferred format for an output means ranks fragments of the *Borrelia burgdorferi* genomic sequences possessing varying degrees of homology to the target sequence or target motif. Such presentation provides a skilled artisan with a ranking of sequences which contain various amounts of the target sequence or target motif and identifies the degree of homology contained in the identified fragment.

A variety of comparing means can be used to compare a target sequence or target motif with the data storage means to identify sequence fragments of the *Borrelia burgdorferi* genome. In the present examples, implementing software which implement the BLAST and BLAZE algorithms, described in Altschul *et al.*, *J. Mol. Biol. 215:* 403-410 (1990), is used to identify open reading frames within the *Borrelia burgdorferi* genome. A skilled artisan can readily recognize that any one of the publicly available homology search programs can be used as the search means for the computer-based systems of the present invention. Of course, suitable proprietary systems that may be known to those of skill also may be employed in this regard.

Figure 1 provides a block diagram of a computer system illustrative of embodiments of this aspect of present invention. The computer system 102 includes a processor 106 connected to a bus 104. Also connected to the bus 104 are a main memory 108 (preferably implemented as random access memory, RAM) and a variety of secondary storage devices 110, such as a hard drive 112 and a removable medium storage device 114. The removable medium storage device

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114 may represent, for example, a floppy disk drive, a CD-ROM drive, a magnetic tape drive, etc. A removable storage medium 116 (such as a floppy disk, a compact disk, a magnetic tape, etc.) containing control logic and/or data recorded therein may be inserted into the removable medium storage device 114. The computer system 102 includes appropriate software for reading the control logic and/or the data from the removable medium storage device 114, once it is inserted into the removable medium storage device 114.

A nucleotide sequence of the present invention may be stored in a well known manner in the main memory 108, any of the secondary storage devices 110, and/or a removable storage medium 116. During execution, software for accessing and processing the genomic sequence (such as search tools, comparing tools, *etc.*) reside in main memory 108, in accordance with the requirements and operating parameters of the operating system, the hardware system and the software program or programs.

BIOCHEMICAL EMBODIMENTS

Other embodiments of the present invention are directed to isolated fragments of the *Borrelia burgdorferi* genome. The fragments of the *Borrelia burgdorferi* genome of the present invention include, but are not limited to fragments which encode peptides, hereinafter open reading frames (ORFs), fragments which modulate the expression of an operably linked ORF, hereinafter expression modulating fragments (EMFs) and fragments which can be used to diagnose the presence of *Borrelia burgdorferi* in a sample, hereinafter diagnostic fragments (DFs).

As used herein, an "isolated nucleic acid molecule" or an "isolated fragment of the *Borrelia burgdorferi* genome" refers to a nucleic acid molecule possessing a specific nucleotide sequence which has been subjected to purification means to reduce, from the composition, the number of compounds which are normally associated with the composition. Particularly, the term refers to the nucleic acid molecules having the sequences set out in SEQ ID NOS: 1-155, to representative fragments thereof as described above including ORF IDs and ORFs, to polynucleotides at least 95%, preferably at least 96%, 97%, 98%, or 99% and especially preferably at least 99.9% identical in sequence thereto, also as set out above.

A variety of purification means can be used to generate the isolated fragments of the present invention. These include, but are not limited to methods which separate constituents of a solution based on charge, solubility, or size.

In one embodiment, *Borrelia burgdorferi* DNA can be enzymatically sheared to produce fragments of 15-20 kb in length. These fragments can then be used to generate a *Borrelia burgdorferi* library by inserting them into lambda clones as described in the Examples below. Primers flanking, for example, an ORF, such as those enumerated in Tables 1-6 can then be generated using nucleotide sequence information provided in SEQ ID NOS: 1-155. Well known and routine techniques of PCR cloning then can be used to isolate the ORF from the lambda DNA library or *Borrelia burgdorferi* genomic DNA. Thus, given the availability of SEQ ID NOS:1-

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155, the information in Tables 1-6, and the information that may be obtained readily by analysis of the sequences of SEQ ID NOS:1-155 using methods set out above, those of skill will be enabled by the present disclosure to isolate any ORF-containing or other nucleic acid fragment of the present invention.

The isolated nucleic acid molecules of the present invention include, but are not limited to single stranded and double stranded DNA, and single stranded RNA. For purposes of numbering and reference to polynucleotide and polypeptide sequences the entire sequence of each sequence of SEQ ID NOS:1-155 is included with the first nucleotide being position 1. Therefore, for reference purposes the numbering used in the present invention is that provided in the sequence listing for SEQ ID NOS:1-155.

As used herein, an open reading frame (ORF), means a series of nucleotide triplets coding for amino acid residues without any termination codons and is a sequence translatable into protein. Further, unless specified, the term "ORF" for each ORF ID is defined by the termination codon at the 3' end and the 5' most methionine codon, at the 5' end, in frame with said 3' termination codon. Unless specified, the term "ORF" also refers to a particular polypeptide sequence defined by the ORF polynucleotide sequence, wherein the N-terminus is defined by the 5' most methionine codon in frame with the termination codon at the 3' end of the ORF ID and the C-terminus is defined by the last codon before the said 3' termination codon. As used herein, an ORF ID represents a sequence without any internal termination codons flanked by termination codons.

Tables 1-6 list ORF IDs in the *Borrelia burgdorferi* genomic contigs of the present invention that were identified as putative coding regions by the GeneMark software using organism-specific second-order Markov probability transition matrices. It will be appreciated that other criteria can be used, in accordance with well known analytical methods, such as those discussed herein, to generate more inclusive, more restrictive, or more selective lists.

The *B. burgdorferi* genome consists of one large linear chromosome containing approximately two thirds of its genetic material and multiple extrachromosomal elements (approximately 15) containing the remaining one third of its genetic material. SEQ ID NO:1 (Contig ID 1) is the complete sequence of the large linear *B. burgdorferi* chromosome. SEQ ID NOS:2-155 (Contig ID 2-155 respectively) are fragments (contigs) of the extrachromosomal elements. Tables 1-3 below relate only to SEQ ID NO:1. Tables 4-6 relate to the extrachromosomal elements (SEQ ID NOS:2-155).

Table 1 sets out ORF IDs in the *Borrelia burgdorferi* chromosome of the present invention that cover a continuous region of at least 50 bases are 95% or more identical (by BLAST analysis using default parameters) to a nucleotide sequence available through GenBank in July, 1997.

Table 2 sets out ORF IDs in the *Borrelia burgdorferi* chromosome of the present invention that are not in Table 1 and match, with a BLASTP probability score of 0.01 or less, a polypeptide sequence available through GenBank in July, 1997.

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Table 3 sets out ORF IDs in the *Borrelia burgdorferi* chromosome of the present invention that do not match significantly, by BLASTP analysis, a polypeptide sequence available through GenBank in July, 1997.

Table 4 sets out ORF IDs in the *Borrelia burgdorferi* extrachromosomal element contigs of the present invention that over a continuous region of at least 50 bases are 95% or more identical (by BLAST analysis) to a nucleotide sequence available through GenBank in July, 1997.

Table 5 sets out ORF IDs in the *Borrelia burgdorferi* extrachromosomal element contigs of the present invention that are not in Table 1 and match, with a BLASTP probability score of 0.01 or less, a polypeptide sequence available through GenBank in July, 1997.

Table 6 sets out ORF IDs in the *Borrelia burgdorferi* extrachromosomal element contigs of the present invention that do not match significantly, by BLASTP analysis, a polypeptide sequence available through GenBank in July, 1997.

In each table, the first and second columns identify the ORF ID by, respectively, contig number and ORF ID number within the contig; the third column indicates the first nucleotide of the ORF ID, counting from the 5' end of the contig strand; and the fourth column indicates the last nucleotide of the ORF ID, counting from the 5' end of the contig strand.

In Tables 1, 2, 4 and 5, column five, lists the Reference for the closest matching sequence available through GenBank. These reference numbers are the database accession numbers commonly used by those of skill in the art, who will be familiar with their denominators. Descriptions of the nomenclature are available from the National Center for Biotechnology Information. Column seven provides the BLAST identity score from the comparison of the ORF ID and the homologous gene; and column nine indicates the length in nucleotides of the highest scoring segment pair identified by the BLAST identity analysis.

The concepts of percent identity and percent similarity of two polypeptide sequences is well understood in the art. For example, two polypeptides 10 amino acids in length which differ at three amino acid positions (e.g., at positions 1, 3 and 5) are said to have a percent identity of 70%. However, the same two polypeptides would be deemed to have a percent similarity of 80% if, for example at position 5, the amino acids moieties, although not identical, were "similar" (i.e., possessed similar biochemical characteristics). As is known in the art, substitution of one amino acid for a "similar" amino acid is a conservative substitution. Generally, proteins are highly tolerant of conservative substitutions. Many programs for analysis of nucleotide or amino acid sequence similarity, such as fasta and BLAST specifically list percent identity of a matching region as an output parameter. Thus, for instance, Tables 1, 2, 4 and 5 herein enumerate the percent identity and similarity of the highest scoring segment pair in each ORF and its listed relative. Further details concerning the algorithms and criteria used for homology searches are provided below and are described in the pertinent literature highlighted by the citations provided below.

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It will be appreciated that other criteria can be used to generate more inclusive and more exclusive listings of the types set out in the tables. As those of skill will appreciate, narrow and broad searches both are useful. Thus, a skilled artisan can readily identify ORFs in contigs of the *Borrelia burgdorferi* genome other than those listed in Tables 1-6, such as ORFs which are overlapping or encoded by the opposite strand of an identified ORF in addition to those ascertainable using the computer-based systems of the present invention.

As used herein, an "expression modulating fragment," EMF, means a series of nucleotide molecules which modulates the expression of an operably linked ORF or EMF.

As used herein, a sequence is said to "modulate the expression of an operably linked sequence" when the expression of the sequence is altered by the presence of the EMF. EMFs include, but are not limited to, promoters, and promoter modulating sequences (inducible elements). One class of EMFs are fragments which induce the expression or an operably linked ORF in response to a specific regulatory factor or physiological event.

EMF sequences can be identified within the contigs of the *Borrelia burgdorferi* genome by their proximity to the ORFs provided in Tables 1-6. An intergenic segment, or a fragment of the intergenic segment, from about 10 to 200 nucleotides in length, taken from any one of the ORFs of Tables 1-6 will modulate the expression of an operably linked ORF in a fashion similar to that found with the naturally linked ORF sequence. As used herein, an "intergenic segment" refers to fragments of the *Borrelia burgdorferi* genome which are between two ORF(s) herein described. EMFs also can be identified using known EMFs as a target sequence or target motif in the computer-based systems of the present invention. Further, the two methods can be combined and used together.

The presence and activity of an EMF can be confirmed using an EMF trap vector. An EMF trap vector contains a cloning site linked to a marker sequence. A marker sequence encodes an identifiable phenotype, such as antibiotic resistance or a complementing nutrition auxotrophic factor, which can be identified or assayed when the EMF trap vector is placed within an appropriate host under appropriate conditions. As described above, a EMF will modulate the expression of an operably linked marker sequence. A more detailed discussion of various marker sequences is provided below. A sequence which is suspected as being an EMF is cloned in all three reading frames in one or more restriction sites upstream from the marker sequence in the EMF trap vector. The vector is then transformed into an appropriate host using known procedures and the phenotype of the transformed host in examined under appropriate conditions. As described above, an EMF will modulate the expression of an operably linked marker sequence.

As used herein, a "diagnostic fragment," DF, means a series of nucleotide molecules which selectively hybridize to *Borrelia burgdorferi* sequences. DFs can be readily identified by identifying unique sequences within contigs of the *Borrelia burgdorferi* genome, such as by using well-known computer analysis software, and by generating and testing probes or

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amplification primers consisting of the DF sequence in an appropriate diagnostic format which determines amplification or hybridization selectivity.

The sequences falling within the scope of the present invention are not limited to the specific sequences herein described, but also include allelic and species variations thereof. Allelic and species variations can be routinely determined by comparing the sequences provided in SEQ ID NOS:1-155, ORF IDs and ORFs within, a representative fragment thereof, or a nucleotide sequence at least 99% and preferably 99.9% identical to SEQ ID NOS: 1-155, ORF IDs and ORFs within, with a sequence from another isolate of the same species. Furthermore, to accommodate codon variability, the invention includes nucleic acid molecules coding for the same amino acid sequences as do the specific ORFs disclosed herein. In other words, in the coding region of an ORF, substitution of one codon for another which encodes the same amino acid is expressly contemplated.

Any specific sequence disclosed herein can be readily screened for errors by resequencing a particular fragment, such as an ORF, in both directions (i.e., sequence both strands). Alternatively, error screening can be performed by sequencing corresponding polynucleotides of *Borrelia burgdorferi* origin isolated by using part or all of the fragments in question as a probe or primer.

Each of the ORF IDs and ORFs of the *Borrelia burgdorferi* genome disclosed in Tables 1-6, and the EMFs found 5' to the ORF IDs, can be used as polynucleotide reagents in numerous ways. For example, the sequences can be used as diagnostic probes or diagnostic amplification primers to detect the presence of a specific microbe in a sample, particularly *Borrelia burgdorferi*. Especially preferred in this regard are ORF IDs and ORFs such as those of Tables 3 and 6, which do not match previously characterized sequences from other organisms and thus are most likely to be highly selective for *Borrelia burgdorferi*. Also particularly preferred are ORF IDs and ORFs that can be used to distinguish between strains of *Borrelia burgdorferi*, particularly those that distinguish medically important strain, such as drug-resistant strains.

In addition, the fragments of the present invention, as broadly described, can be used to control gene expression through triple helix formation or antisense DNA or RNA, both of which methods are based on the binding of a polynucleotide sequence to DNA or RNA. Triple helix-formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Information from the sequences of the present invention can be used to design antisense and triple helix-forming oligonucleotides. Polynucleotides suitable for use in these methods are usually 20 to 40 bases in length and are designed to be complementary to a region of the gene involved in transcription, for triple-helix formation, or to the mRNA itself, for antisense inhibition. Both techniques have been demonstrated to be effective in model systems, and the requisite techniques are well known and involve routine procedures. Triple helix techniques are discussed in, for example, Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991). Antisense techniques in general are discussed in, for instance, Okano,

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J. Neurochem. 56:560 (1991) and Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988)).

The present invention further provides recombinant constructs comprising one or more fragments of the *Borrelia burgdorferi* genomic fragments and contigs of the present invention. Certain preferred recombinant constructs of the present invention comprise a vector, such as a plasmid or viral vector, into which a fragment of the *Borrelia burgdorferi* genome has been inserted, in a forward or reverse orientation. In the case of a vector comprising one of the ORF IDs or ORFs of the present invention, the vector may further comprise regulatory sequences, including for example, a promoter, operably linked to the ORF ID or ORF. For vectors comprising the EMFs of the present invention, the vector may further comprise a marker sequence or heterologous ORF ID or ORF operably linked to the EMF.

Large numbers of suitable vectors and promoters are known to those of skill in the art and are commercially available for generating the recombinant constructs of the present invention. The following vectors are provided by way of example. Useful bacterial vectors include phagescript, PsiX174, pBluescript SK, pBS KS, pNH8a, pNH16a, pNH18a, pNH46a (available from Stratagene); pTrc99A, pKK223-3, pKK233-3, pDR540, pRIT5 (available from Pharmacia); pQE vectors (available from Promega). Useful eukaryotic vectors include pWLneo, pSV2cat, pOG44, pXT1, pSG (available from Stratagene) pSVK3, pBPV, pMSG, pSVL (available from Pharmacia).

Promoter regions can be selected from any desired gene using CAT (chloramphenicol transferase) vectors or other vectors with selectable markers. Two appropriate vectors are pKK232-8 and pCM7. Particular named bacterial promoters include lacI, lacZ, T3, T7, gpt, lambda PR, and trc. Eukaryotic promoters include CMV immediate early, HSV thymidine kinase, early and late SV40, LTRs from retrovirus, and mouse metallothionein- I. Selection of the appropriate vector and promoter is well within the level of ordinary skill in the art.

The present invention further provides host cells containing any one of the isolated fragments of the *Borrelia burgdorferi* genomic fragments and contigs of the present invention, wherein the fragment has been introduced into the host cell using known methods. The host cell can be a higher eukaryotic host cell, such as a mammalian cell, a lower eukaryotic host cell, such as a yeast cell, or a procaryotic cell, such as a bacterial cell.

A polynucleotide of the present invention, such as a recombinant construct comprising an ORF of the present invention, may be introduced into the host by a variety of well established techniques that are standard in the art, such as calcium phosphate transfection, DEAE, dextran mediated transfection and electroporation, which are described in, for instance, Davis, L. et al., BASIC METHODS IN MOLECULAR BIOLOGY (1986).

A host cell containing one of the fragments of the *Borrelia burgdorferi* genomic fragments and contigs of the present invention, can be used in conventional manners to produce the gene product encoded by the isolated fragment (in the case of an ORF) or can be used to produce a heterologous protein under the control of the EMF.

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The present invention further provides isolated polypeptides encoded by the nucleic acid fragments of the present invention or by degenerate variants of the nucleic acid fragments of the present invention. By "degenerate variant" is intended nucleotide fragments which differ from a nucleic acid fragment of the present invention (e.g., an ORF) by nucleotide sequence but, due to the degeneracy of the Genetic Code, encode an identical polypeptide sequence.

Preferred nucleic acid fragments of the present invention are the ORF IDs depicted in Tables 2, 3, 5 and 6, and ORFs witin, which encode proteins.

A variety of methodologies known in the art can be utilized to obtain any one of the isolated polypeptides or proteins of the present invention. At the simplest level, the amino acid sequence can be synthesized using commercially available peptide synthesizers. This is particularly useful in producing small peptides and fragments of larger polypeptides. Such short fragments as may be obtained most readily by synthesis are useful, for example, in generating antibodies against the native polypeptide, as discussed further below.

In an alternative method, the polypeptide or protein is purified from bacterial cells which naturally produce the polypeptide or protein. One skilled in the art can readily employ well-known methods for isolating polypeptides and proteins to isolate and purify polypeptides or proteins of the present invention produced naturally by a bacterial strain, or by other methods. Methods for isolation and purification that can be employed in this regard include, but are not limited to, immunochromatography, HPLC, size-exclusion chromatography, ion-exchange chromatography, and immuno-affinity chromatography.

The polypeptides and proteins of the present invention also can be purified from cells which have been altered to express the desired polypeptide or protein. As used herein, a cell is said to be altered to express a desired polypeptide or protein when the cell, through genetic manipulation, is made to produce a polypeptide or protein which it normally does not produce or which the cell normally produces at a lower level. Those skilled in the art can readily adapt procedures for introducing and expressing either recombinant or synthetic sequences into eukaryotic or prokaryotic cells in order to generate a cell which produces one of the polypeptides or proteins of the present invention.

The polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of the *B. burgdorferi* polypeptide can be substantially purified by the one-step method described by Smith et al. (1988) Gene 67:31-40. Polypeptides of the invention also can be purified from natural or recombinant sources using antibodies directed against the polypeptides of the invention in methods which are well known in the art of protein purification.

The invention further provides for isolated *B. burgdorferi* polypeptides comprising an amino acid sequence selected from the group including: (a) the amino acid sequence of a full-length *B. burgdorferi* polypeptide having the complete amino acid sequence from the first methionine codon to the termination codon of each sequence listed in SEQ ID NOS:1-155, wherein said termination codon is at the end of each SEQ ID NO: and said first methionine is the

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first methionine in frame with said termination codon; and (b) the amino acid sequence of a full-length *B. burgdorferi* polypeptide having the complete amino acid sequence in (a) excepting the N-terminal methionine.

The polypeptides of the present invention also include polypeptides having an amino acid sequence at least 80% identical, more preferably at least 90% identical, and still more preferably 95%, 96%, 97%, 98% or 99% identical to those described in (a) and (b) above.

The present invention is further directed to polynucleotides encoding portions or fragments of the amino acid sequences described herein as well as to portions or fragments of the isolated amino acid sequences described herein. Fragments include portions of the amino acid sequences described herein at least 5 contiguous amino acid in length and selected from any two integers, one of which representing an N-terminal position and another representing a C-terminal position. The initiation codon of the ORFs of the present invention is position 1. The initiation codon (positon 1) for purposes of the present invention is the first methionine codon of each ORF ID which is in frame with the termination codon at the end of each said sequence. Every combination of a N-terminal and C-terminal position that a fragment at least 5 contiguous amino acid residues in length could occupy, on any given ORF is included in the invention, i.e., from initiation codon up to the termination codon. "At least" means a fragment may be 5 contiguous amino acid residues in length or any integer between 5 and the number of residues in an ORF, minus 1. Therefore, included in the invention are contiguous fragments specified by any Nterminal and C-terminal positions of amino acid sequence set forth in SEQ ID NOS:1-155 or Tables 1-6 wherein the contiguous fragment is any integer between 5 and the number of residues in an ORF minus 1.

Further, the invention includes polypeptides comprising fragments specified by size, in amino acid residues, rather than by N-terminal and C-terminal positions. The invention includes any fragment size, in contiguous amino acid residues, selected from integers between 5 and the number of residues in an ORF, minus 1. Preferred sizes of contiguous polypeptide fragments include about 5 amino acid residues, about 10 amino acid residues, about 20 amino acid residues, about 30 amino acid residues, about 40 amino acid residues, about 50 amino acid residues, about 100 amino acid residues, about 200 amino acid residues, about 300 amino acid residues, and about 400 amino acid residues. The preferred sizes are, of course, meant to exemplify, not limit, the present invention as all size fragments representing any integer between 5 and the number of residues in a full length sequence minus 1 are included in the invention. The present invention also provides for the exclusion of any fragments specified by N-terminal and C-terminal positions or by size in amino acid residues as described above. Any number of fragments specified by N-terminal and C-terminal positions or by size in amino acid residues as described above may be excluded.

The above fragments need not be active since they would be useful, for example, in immunoassays, in epitope mapping, epitope tagging, to generate antibodies to a particular portion of the protein, as vaccines, and as molecular weight markers.

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Further polypeptides of the present invention include polypeptides which have at least 90% similarity, more preferably at least 95% similarity, and still more preferably at least 96%, 97%, 98% or 99% similarity to those described above.

A further embodiment of the invention relates to a polypeptide which comprises the amino acid sequence of a *B. burgdorferi* polypeptide having an amino acid sequence which contains at least one conservative amino acid substitution, but not more than 50 conservative amino acid substitutions, not more than 40 conservative amino acid substitutions, not more than 30 conservative amino acid substitutions, and not more than 20 conservative amino acid substitutions. Also provided are polypeptides which comprise the amino acid sequence of a *B. burgdorferi* polypeptide, having at least one, but not more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 conservative amino acid substitutions.

By a polypeptide having an amino acid sequence at least, for example, 95% "identical" to a query amino acid sequence of the present invention, it is intended that the amino acid sequence of the subject polypeptide is identical to the query sequence except that the subject polypeptide sequence may include up to five amino acid alterations per each 100 amino acids of the query amino acid sequence. In other words, to obtain a polypeptide having an amino acid sequence at least 95% identical to a query amino acid sequence, up to 5% of the amino acid residues in the subject sequence may be inserted, deleted, (indels) or substituted with another amino acid. These alterations of the reference sequence may occur at the amino or carboxy terminal positions of the reference amino acid sequence or anywhere between those terminal positions, interspersed either individually among residues in the reference sequence or in one or more contiguous groups within the reference sequence.

As a practical matter, whether any particular polypeptide is at least 90%, 95%, 96%, 97%, 98% or 99% identical to the ORF amino acid sequences encoded by the sequences of SEQ ID NOS:1-155, as described hererin, can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al., (1990) Comp. App. Biosci. 6:237-245. In a sequence alignment the query and subject sequences are both amino acid sequences. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB amino acid alignment are:

Matrix=PAM 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Window Size=sequence length, Gap Penalty=5, Gap Size Penalty=0.05, Window Size=500 or the length of the subject amino acid sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence due to N- or C-terminal deletions, not because of internal deletions, the results, in percent identity, must be manually corrected. This is because the FASTDB program does not account for N- and C-terminal truncations of the subject sequence when calculating global percent identity. For subject

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340:245-246.

sequences truncated at the N- and C-termini, relative to the query sequence, the percent identity is corrected by calculating the number of residues of the query sequence that are N- and C-terminal of the subject sequence, which are not matched/aligned with a corresponding subject residue, as a percent of the total bases of the query sequence. Whether a residue is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This final percent identity score is what is used for the purposes of the present invention. Only residues to the N- and C-termini of the subject sequence, which are not matched/aligned with the query sequence, are considered for the purposes of manually adjusting the percent identity score. That is, only query amino acid residues outside the farthest N- and C-terminal residues of the subject sequence.

For example, a 90 amino acid residue subject sequence is aligned with a 100 residue query sequence to determine percent identity. The deletion occurs at the N-terminus of the subject sequence and therefore, the FASTDB alignment does not match/align with the first 10 residues at the N-terminus. The 10 unpaired residues represent 10% of the sequence (number of residues at the N- and C- termini not matched/total number of residues in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 residues were perfectly matched the final percent identity would be 90%. In another example, a 90 residue subject sequence is compared with a 100 residue query sequence. This time the deletions are internal so there are no residues at the N- or C-termini of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only residue positions outside the N- and C-terminal ends of the subject sequence, as displayed in the FASTDB alignment, which are not matched/aligned with the query sequence are manually corrected. No other manual corrections are to made for the purposes of the present invention.

The above polypeptide sequences are included irrespective of whether they have their normal biological activity. This is because even where a particular polypeptide molecule does not have biological activity, one of skill in the art would still know how to use the polypeptide, for instance, as a vaccine or to generate antibodies. Other uses of the polypeptides of the present invention that do not have *B. burgdorferi* activity include, *inter alia*, as epitope tags, in epitope mapping, and as molecular weight markers on SDS-PAGE gels or on molecular sieve gel filtration columns using methods known to those of skill in the art.

As described below, the polypeptides of the present invention can also be used to raise polyclonal and monoclonal antibodies, which are useful in assays for detecting *B. burgdorferi* protein expression or as agonists and antagonists capable of enhancing or inhibiting *B. burgdorferi* protein function. Further, such polypeptides can be used in the yeast two-hybrid system to "capture" *B. burgdorferi* protein binding proteins which are also candidate agonists and antagonists according to the present invention. *See, e.g.*, Fields et al. (1989) Nature

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Any host/vector system can be used to express one or more of the ORFs of the present invention. These include, but are not limited to, eukaryotic hosts such as HeLa cells, CV-1 cell, COS cells, and Sf9 cells, as well as prokaryotic host such as *E. coli* and *B. subtilis*. The most preferred cells are those which do not normally express the particular polypeptide or protein or which expresses the polypeptide or protein at low natural level.

"Recombinant," as used herein, means that a polypeptide or protein is derived from recombinant (e.g., microbial or mammalian) expression systems. "Microbial" refers to recombinant polypeptides or proteins made in bacterial or fungal (e.g., yeast) expression systems. As a product, "recombinant microbial"defines a polypeptide or protein essentially free of native endogenous substances and unaccompanied by associated native glycosylation. Polypeptides or proteins expressed in most bacterial cultures, e.g., E. coli, will be free of glycosylation modifications; polypeptides or proteins expressed in yeast will have a glycosylation pattern different from that expressed in mammalian cells.

"Nucleotide sequence" refers to a heteropolymer of deoxyribonucleotides. Generally, DNA segments encoding the polypeptides and proteins provided by this invention are assembled from fragments of the *Borrelia burgdorferi* genome and short oligonucleotide linkers, or from a series of oligonucleotides, to provide a synthetic gene which is capable of being expressed in a recombinant transcriptional unit comprising regulatory elements derived from a microbial or viral operon.

Recombinant expression vehicle or vector" refers to a plasmid or phage or virus or vector, for expressing a polypeptide from a DNA (RNA) sequence. The expression vehicle can comprise a transcriptional unit comprising an assembly of (1) a genetic regulatory elements necessary for gene expression in the host, including elements required to initiate and maintain transcription at a level sufficient for suitable expression of the desired polypeptide, including, for example, promoters and, where necessary, an enhancer and a polyadenylation signal; (2) a structural or coding sequence which is transcribed into mRNA and translated into protein, and (3) appropriate signals to initiate translation at the beginning of the desired coding region and terminate translation at its end. Structural units intended for use in yeast or eukaryotic expression systems preferably include a leader sequence enabling extracellular secretion of translated protein by a host cell. Alternatively, where recombinant protein is expressed without a leader or transport sequence, it may include an N-terminal methionine residue. This residue may or may not be subsequently cleaved from the expressed recombinant protein to provide a final product.

"Recombinant expression system" means host cells which have stably integrated a recombinant transcriptional unit into chromosomal DNA or carry the recombinant transcriptional unit extra chromosomally. The cells can be prokaryotic or eukaryotic. Recombinant expression systems as defined herein will express heterologous polypeptides or proteins upon induction of the regulatory elements linked to the DNA segment or synthetic gene to be expressed.

Mature proteins can be expressed in mammalian cells, yeast, bacteria, or other cells under the control of appropriate promoters. Cell-free translation systems can also be employed to

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produce such proteins using RNAs derived from the DNA constructs of the present invention. Appropriate cloning and expression vectors for use with prokaryotic and eukaryotic hosts are described in Sambrook et al., Molecular Cloning: A Laboratory Manual, 2nd Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York (1989), the disclosure of which is hereby incorporated by reference in its entirety.

Generally, recombinant expression vectors will include origins of replication and selectable markers permitting transformation of the host cell, e.g., the ampicillin resistance gene of E. coli and S. cerevisiae TRP1 gene, and a promoter derived from a highly expressed gene to direct transcription of a downstream structural sequence. Such promoters can be derived from operons encoding glycolytic enzymes such as 3- phosphoglycerate kinase (PGK), alpha-factor, acid phosphatase, or heat shock proteins, among others. The heterologous structural sequence is assembled in appropriate phase with translation initiation and termination sequences, and preferably, a leader sequence capable of directing secretion of translated protein into the periplasmic space or extracellular medium. Optionally, the heterologous sequence can encode a fusion protein including an N-terminal identification peptide imparting desired characteristics, e.g., stabilization or simplified purification of expressed recombinant product.

Useful expression vectors for bacterial use are constructed by inserting a structural DNA sequence encoding a desired protein together with suitable translation initiation and termination signals in operable reading phase with a functional promoter. The vector will comprise one or more phenotypic selectable markers and an origin of replication to ensure maintenance of the vector and, when desirable, provide amplification within the host.

Suitable prokaryotic hosts for transformation include strains of *E. coli*, *B. subtilis*, *Salmonella typhimurium* and various species within the genera *Pseudomonas* and *Streptomyces*. Others may, also be employed as a matter of choice.

As a representative but non-limiting example, useful expression vectors for bacterial use can comprise a selectable marker and bacterial origin of replication derived from commercially available plasmids comprising genetic elements of the well known cloning vector pBR322 (ATCC 37017). Such commercial vectors include, for example, pKK223-3 (available form Pharmacia Fine Chemicals, Uppsala, Sweden) and GEM 1 (available from Promega Biotec, Madison, WI, USA). These pBR322 "backbone" sections are combined with an appropriate promoter and the structural sequence to be expressed.

Following transformation of a suitable host strain and growth of the host strain to an appropriate cell density, the selected promoter, where it is inducible, is derepressed or induced by appropriate means (e.g., temperature shift or chemical induction) and cells are cultured for an additional period to provide for expression of the induced gene product. Thereafter cells are typically harvested, generally by centrifugation, disrupted to release expressed protein, generally by physical or chemical means, and the resulting crude extract is retained for further purification.

Various mammalian cell culture systems can also be employed to express recombinant protein. Examples of mammalian expression systems include the COS-7 lines of monkey kidney

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fibroblasts, described in Gluzman, Cell 23:175 (1981), and other cell lines capable of expressing a compatible vector, for example, the C127, 3T3, CHO, HeLa and BHK cell lines.

Mammalian expression vectors will comprise an origin of replication, a suitable promoter and enhancer, and also any necessary ribosome binding sites, polyadenylation site, splice donor and acceptor sites, transcriptional termination sequences, and 5' flanking nontranscribed sequences. DNA sequences derived from the SV40 viral genome, for example, SV40 origin, early promoter, enhancer, splice, and polyadenylation sites may be used to provide the required nontranscribed genetic elements.

Recombinant polypeptides and proteins produced in bacterial culture is usually isolated by initial extraction from cell pellets, followed by one or more salting-out, aqueous ion exchange or size exclusion chromatography steps. Microbial cells employed in expression of proteins can be disrupted by any convenient method, including freeze-thaw cycling, sonication, mechanical disruption, or use of cell lysing agents. Protein refolding steps can be used, as necessary, in completing configuration of the mature protein. Finally, high performance liquid chromatography (HPLC) can be employed for final purification steps.

The present invention further includes isolated polypeptides, proteins and nucleic acid molecules which are substantially equivalent to those herein described. As used herein, substantially equivalent can refer both to nucleic acid and amino acid sequences, for example a mutant sequence, that varies from a reference sequence by one or more substitutions, deletions, or additions, the net effect of which does not result in an adverse functional dissimilarity between reference and subject sequences. Particularly preferred in this regard are conservative substitutions, known to those of skill in the art. For purposes of the present invention, sequences having equivalent biological activity, and equivalent expression characteristics are considered substantially equivalent. For purposes of determining equivalence, truncation of the mature sequence (e.g., removal of leader sequence(s)) should be disregarded.

The invention further provides methods of obtaining homologs from other strains of Borrelia burgdorferi, of the fragments of the Borrelia burgdorferi genome of the present invention and homologs of the proteins encoded by the ORFs of the present invention. As used herein, a sequence or protein of Borrelia burgdorferi is defined as a homolog of a fragment of the Borrelia burgdorferi fragments or contigs or a protein encoded by one of the ORFs of the present invention, if it shares significant homology to one of the fragments of the Borrelia burgdorferi genome of the present invention or a protein encoded by one of the ORFs of the present invention. Specifically, by using the sequence disclosed herein as a probe or as primers, and techniques such as PCR cloning and colony/plaque hybridization, one skilled in the art can obtain homologs.

As used herein, two nucleic acid molecules or proteins are said to "share significant homology" if the two contain regions which possess greater than 85% sequence (amino acid or nucleic acid) homology. Preferred homologs in this regard are those with more than 90% homology. Especially preferred are those with 95% or more homology. Among especially

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preferred homologs those with 96, 97%, 98%, 99% or more homology are particularly preferred. The most preferred homologs among these are those with 99.9% homology or more. It will be understood that, among measures of homology, identity is particularly preferred in this regard.

Region specific primers or probes derived from the nucleotide sequence provided in SEQ ID NOS: 1-155 or from a nucleotide sequence at least 95%, particularly at least 96%, 97%, 98% or 99%, especially at least 99.5% identical to a sequence of SEQ ID NOS: 1-155 can be used to prime DNA synthesis and PCR amplification, as well as to identify colonies containing cloned DNA encoding a homolog. Methods suitable to this aspect of the present invention are well known and have been described in great detail in many publications such as, for example, Innis et al., PCR Protocols, Academic Press, San Diego, CA (1990)).

When using primers derived from SEQ ID NOS: 1-155 or from a nucleotide sequence having an aforementioned identity to a sequence of SEQ ID NOS:1-155, one skilled in the art will recognize that by employing high stringency conditions (e.g., annealing at 50-60°C in 6X SSPC and 50% formamide, and washing at 50-65°C in 0.5X SSPC) only sequences which are greater than 75% homologous to the primer will be amplified. By employing lower stringency conditions (e.g., hybridizing at 35-37°C in 5X SSPC and 40-45% formamide, and washing at 42°C in 0.5X SSPC), sequences which are greater than 40-50% homologous to the primer will also be amplified.

When using DNA probes derived from SEQ ID NOS:1-155, or from a nucleotide sequence having an aforementioned identity to a sequence of SEQ ID NOS: 1-155, for colony/plaque hybridization, one skilled in the art will recognize that by employing high stringency conditions (e.g., hybridizing at 50-65°C in 5X SSPC and 50% formamide, and washing at 50-65°C in 0.5X SSPC), sequences having regions which are greater than 90% homologous to the probe can be obtained, and that by employing lower stringency conditions (e.g., hybridizing at 35-37°C in 5X SSPC and 40-45% formamide, and washing at 42°C in 0.5X SSPC), sequences having regions which are greater than 35-45% homologous to the probe will be obtained.

Any organism can be used as the source for homologs of the present invention so long as the organism naturally expresses such a protein or contains genes encoding the same. The most preferred organism for isolating homologs are bacteria which are closely related to *Borrelia burgdorferi*.

ILLUSTRATIVE USES OF COMPOSITIONS OF THE INVENTION

Each ORF of the ORF IDs provided in Tables 1, 2, 4 and 5 is identified with a function by homology to a known gene or polypeptide. As a result, one skilled in the art can use the polypeptides of the present invention for commercial, therapeutic and industrial purposes consistent with the type of putative identification of the polypeptide. Such identifications permit one skilled in the art to use the *Borrelia burgdorferi* ORFs in a manner similar to the known type

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of sequences for which the identification is made; for example, to ferment a particular sugar source or to produce a particular metabolite. A variety of reviews illustrative of this aspect of the invention are available, including the following reviews on the industrial use of enzymes, for example, BIOCHEMICAL ENGINEERING AND BIOTECHNOLOGY HANDBOOK, 2nd Ed., MacMillan Publications, Ltd. NY (1991) and BIOCATALYSTS IN ORGANIC SYNTHESES, Tramper *et al.*, Eds., Elsevier Science Publishers, Amsterdam, The Netherlands (1985). A variety of exemplary uses that illustrate this and similar aspects of the present invention are discussed below.

1. Biosynthetic Enzymes

Open reading frames encoding proteins involved in mediating the catalytic reactions involved in intermediary and macromolecular metabolism, the biosynthesis of small molecules, cellular processes and other functions includes enzymes involved in the degradation of the intermediary products of metabolism, enzymes involved in central intermediary metabolism, enzymes involved in respiration, both aerobic and anaerobic, enzymes involved in fermentation, enzymes involved in ATP proton motor force conversion, enzymes involved in broad regulatory function, enzymes involved in amino acid synthesis, enzymes involved in nucleotide synthesis, enzymes involved in cofactor and vitamin synthesis, can be used for industrial biosynthesis.

The various metabolic pathways present in *Borrelia burgdorferi* can be identified based on absolute nutritional requirements as well as by examining the various enzymes identified in Table 1-6 and SEQ ID NOS:1-155.

Of particular interest are polypeptides involved in the degradation of intermediary metabolites as well as non-macromolecular metabolism. Such enzymes include amylases, glucose oxidases, and catalase.

Proteolytic enzymes are another class of commercially important enzymes. Proteolytic enzymes find use in a number of industrial processes including the processing of flax and other vegetable fibers, in the extraction, clarification and depectinization of fruit juices, in the extraction of vegetables' oil and in the maceration of fruits and vegetables to give unicellular fruits. A detailed review of the proteolytic enzymes used in the food industry is provided in Rombouts et al., Symbiosis 21:79 (1986) and Voragen et al. in Biocatalysts In Agricultural Biotechnology, Whitaker et al., Eds., American Chemical Society Symposium Series 389:93 (1989).

The metabolism of sugars is an important aspect of the primary metabolism of *Borrelia burgdorferi*. Enzymes involved in the degradation of sugars, such as, particularly, glucose, galactose, fructose and xylose, can be used in industrial fermentation. Some of the important sugar transforming enzymes, from a commercial viewpoint, include sugar isomerases such as glucose isomerase. Other metabolic enzymes have found commercial use such as glucose oxidases which produces ketogulonic acid (KGA). KGA is an intermediate in the commercial production of ascorbic acid using the Reichstein's procedure, as described in Krueger *et al.*, *Biotechnology* <u>6(A)</u>, Rhine *et al.*, Eds., Verlag Press, Weinheim, Germany (1984).

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Glucose oxidase (GOD) is commercially available and has been used in purified form as well as in an immobilized form for the deoxygenation of beer. See, for instance, Hartmeir et al., Biotechnology Letters 1:21 (1979). The most important application of GOD is the industrial scale fermentation of gluconic acid. Market for gluconic acids which are used in the detergent, textile, leather, photographic, pharmaceutical, food, feed and concrete industry, as described, for example, in Bigelis et al., beginning on page 357 in GENE MANIPULATIONS AND FUNGI; Benett et al., Eds., Academic Press, New York (1985). In addition to industrial applications, GOD has found applications in medicine for quantitative determination of glucose in body fluids recently in biotechnology for analyzing syrups from starch and cellulose hydrosylates. This application is described in Owusu et al., Biochem. et Biophysica. Acta. 872:83 (1986), for instance.

The main sweetener used in the world today is sugar which comes from sugar beets and sugar cane. In the field of industrial enzymes, the glucose isomerase process shows the largest expansion in the market today. Initially, soluble enzymes were used and later immobilized enzymes were developed (Krueger et al., Biotechnology, The Textbook of Industrial Microbiology, Sinauer Associated Incorporated, Sunderland, Massachusetts (1990)). Today, the use of glucose- produced high fructose syrups is by far the largest industrial business using immobilized enzymes. A review of the industrial use of these enzymes is provided by Jorgensen, Starch 40:307 (1988).

Proteinases, such as alkaline serine proteinases, are used as detergent additives and thus represent one of the largest volumes of microbial enzymes used in the industrial sector. Because of their industrial importance, there is a large body of published and unpublished information regarding the use of these enzymes in industrial processes. (See Faultman *et al.*, Acid Proteases Structure Function and Biology, Tang, J., ed., Plenum Press, New York (1977) and Godfrey *et al.*, Industrial Enzymes, MacMillan Publishers, Surrey, UK (1983) and Hepner *et al.*, Report Industrial Enzymes by 1990, Hel Hepner & Associates, London (1986)).

Another class of commercially usable proteins of the present invention are the microbial lipases, described by, for instance, Macrae et al., Philosophical Transactions of the Chiral Society of London 310:227 (1985) and Poserke, Journal of the American Oil Chemist Society 61:1758 (1984). A major use of lipases is in the fat and oil industry for the production of neutral glycerides using lipase catalyzed inter-esterification of readily available triglycerides. Application of lipases include the use as a detergent additive to facilitate the removal of fats from fabrics in the course of the washing procedures.

The use of enzymes, and in particular microbial enzymes, as catalyst for key steps in the synthesis of complex organic molecules is gaining popularity at a great rate. One area of great interest is the preparation of chiral intermediates. Preparation of chiral intermediates is of interest to a wide range of synthetic chemists particularly those scientists involved with the preparation of new pharmaceuticals, agrochemicals, fragrances and flavors. (See Davies et al., Recent Advances in the Generation of Chiral Intermediates Using Enzymes, CRC Press, Boca Raton,

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Florida (1990)). The following reactions catalyzed by enzymes are of interest to organic chemists: hydrolysis of carboxylic acid esters, phosphate esters, amides and nitriles, esterification reactions, trans-esterification reactions, synthesis of amides, reduction of alkanones and oxoalkanates, oxidation of alcohols to carbonyl compounds, oxidation of sulfides to sulfoxides, and carbon bond forming reactions such as the aldol reaction.

When considering the use of an enzyme encoded by one of the ORFs of the present invention for biotransformation and organic synthesis it is sometimes necessary to consider the respective advantages and disadvantages of using a microorganism as opposed to an isolated enzyme. Pros and cons of using a whole cell system on the one hand or an isolated partially purified enzyme on the other hand, has been described in detail by Bud *et al.*, Chemistry in Britain (1987), p. 127.

Amino transferases, enzymes involved in the biosynthesis and metabolism of amino acids, are useful in the catalytic production of amino acids. The advantages of using microbial based enzyme systems is that the amino transferase enzymes catalyze the stereo- selective synthesis of only L-amino acids and generally possess uniformly high catalytic rates. A description of the use of amino transferases for amino acid production is provided by Roselle-David, *Methods of Enzymology 136*:479 (1987).

Another category of useful proteins encoded by the ORFs of the present invention include enzymes involved in nucleic acid synthesis, repair, and recombination.

2. Generation of Antibodies

As described here, the proteins of the present invention, as well as homologs thereof, can be used in a variety of procedures and methods known in the art which are currently applied to other proteins. The proteins of the present invention can further be used to generate an antibody which selectively binds the protein.

B. burgdorferi protein-specific antibodies for use in the present invention can be raised against the intact B. burgdorferi protein or an antigenic polypeptide fragment thereof, which may be presented together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse) or, if it is long enough (at least about 25 amino acids), without a carrier.

As used herein, the term "antibody" (Ab) or "monoclonal antibody" (Mab) is meant to include intact molecules, single chain whole antibodies, and antibody fragments. Antibody fragments of the present invention include Fab and F(ab')2 and other fragments including single-chain Fvs (scFv) and disulfide-linked Fvs (sdFv). Also included in the present invention are chimeric and humanized monoclonal antibodies and polyclonal antibodies specific for the polypeptides of the present invention. The antibodies of the present invention may be prepared by any of a variety of methods. For example, cells expressing a polypeptide of the present invention or an antigenic fragment thereof can be administered to an animal in order to induce the production of sera containing polyclonal antibodies. For example, a preparation of *B. burgdorferi* polypeptide or fragment thereof is prepared and purified to render it substantially free

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of natural contaminants. Such a preparation is then introduced into an animal in order to produce polyclonal antisera of greater specific activity.

In a preferred method, the antibodies of the present invention are monoclonal antibodies or binding fragments thereof. Such monoclonal antibodies can be prepared using hybridoma technology. *See, e.g.*, Harlow et al., ANTIBODIES: A LABORATORY MANUAL, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling, et al., in: MONOCLONAL ANTIBODIES AND T-CELL HYBRIDOMAS 563-681 (Elsevier, N.Y., 1981). Fab and F(ab')2 fragments may be produced by proteolytic cleavage, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')2 fragments). Alternatively, *B. burgdorferi* polypeptide-binding fragments, chimeric, and humanized antibodies can be produced through the application of recombinant DNA technology or through synthetic chemistry using methods known in the art.

Alternatively, additional antibodies capable of binding to the polypeptide antigen of the present invention may be produced in a two-step procedure through the use of anti-idiotypic antibodies. Such a method makes use of the fact that antibodies are themselves antigens, and that, therefore, it is possible to obtain an antibody which binds to a second antibody. In accordance with this method, *B. burgdorferi* polypeptide-specific antibodies are used to immunize an animal, preferably a mouse. The splenocytes of such an animal are then used to produce hybridoma cells, and the hybridoma cells are screened to identify clones which produce an antibody whose ability to bind to the *B. burgdorferi* polypeptide-specific antibody can be blocked by the *B. burgdorferi* polypeptide antigen. Such antibodies comprise anti-idiotypic antibodies to the *B. burgdorferi* polypeptide-specific antibody and can be used to immunize an animal to induce formation of further *B. burgdorferi* polypeptide-specific antibodies.

Antibodies and fragements thereof of the present invention may be described by the portion of a polypeptide of the present invention recognized or specifically bound by the antibody. Antibody binding fragements of a polypeptide of the present invention may be described or specified in the same manner as for polypeptide fragements discussed above., i.e, by N-terminal and C-terminal positions or by size in contiguous amino acid residues. Any number of antibody binding fragments, of a polypeptide of the present invention, specified by N-terminal and C-terminal positions or by size in amino acid residues, as described above, may also be excluded from the present invention. Therefore, the present invention includes antibodies the specifically bind a particuarly discribed fragement of a polypeptide of the present invention and allows for the exclusion of the same.

Antibodies and fragements thereof of the present invention may also be described or specified in terms of their cross-reactivity. Antibodies and fragements that do not bind polypeptides of any other species of *Borrelia* other than *B. burgdorferi* are included in the present invention. Likewise, antibodies and fragements that bind only species of *Borrelia*, i.e. antibodies and fragements that do not bind bacteria from any genus other than *Borrelia*, are included in the present invention.

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3. Epitope-Bearing Portions

In another aspect, the invention provides peptides and polypeptides comprising epitope-bearing portions of the *B. burgdorferi* polypeptides of the present invention. These epitopes are immunogenic or antigenic epitopes of the polypeptides of the present invention. An "immunogenic epitope" is defined as a part of a protein that elicits an antibody response when the whole protein or polypeptide is the immunogen. These immunogenic epitopes are believed to be confined to a few loci on the molecule. On the other hand, a region of a protein molecule to which an antibody can bind is defined as an "antigenic determinant" or "antigenic epitope." The number of immunogenic epitopes of a protein generally is less than the number of antigenic epitopes. *See, e.g.,* Geysen, et al. (1983) Proc. Natl. Acad. Sci. USA 81:3998- 4002. Amino acid residues comprising anigenic epitopes may be determined by algorithms such as the the Jameson-Wolf analysis or similar algorithms or by *in vivo* testing for an antigenic response using the methods described herein or those known in the art.

As to the selection of peptides or polypeptides bearing an antigenic epitope (*i.e.*, that contain a region of a protein molecule to which an antibody can bind), it is well known in that art that relatively short synthetic peptides that mimic part of a protein sequence are routinely capable of eliciting an antiserum that reacts with the partially mimicked protein. *See, e.g.*, Sutcliffe, et al., (1983) Science 219:660-666. Peptides capable of eliciting protein-reactive sera are frequently represented in the primary sequence of a protein, can be characterized by a set of simple chemical rules, and are confined neither to immunodominant regions of intact proteins (*i.e.*, immunogenic epitopes) nor to the amino or carboxyl terminals. Peptides that are extremely hydrophobic and those of six or fewer residues generally are ineffective at inducing antibodies that bind to the mimicked protein; longer, peptides, especially those containing proline residues, usually are effective. *See*, Sutcliffe, et al., *supra*, p. 661. For instance, 18 of 20 peptides designed according to these guidelines, containing 8-39 residues covering 75% of the sequence of the influenza virus hemagglutinin HA1 polypeptide chain, induced antibodies that reacted with the HA1 protein or intact virus; and 12/12 peptides from the MuLV polymerase and 18/18 from the rabies glycoprotein induced antibodies that precipitated the respective proteins.

Antigenic epitope-bearing peptides and polypeptides of the invention are therefore useful to raise antibodies, including monoclonal antibodies, that bind specifically to a polypeptide of the invention. Thus, a high proportion of hybridomas obtained by fusion of spleen cells from donors immunized with an antigen epitope-bearing peptide generally secrete antibody reactive with the native protein. *See* Sutcliffe, et al., *supra*, p. 663. The antibodies raised by antigenic epitope-bearing peptides or polypeptides are useful to detect the mimicked protein, and antibodies to different peptides may be used for tracking the fate of various regions of a protein precursor which undergoes post-translational processing. The peptides and anti-peptide antibodies may be used in a variety of qualitative or quantitative assays for the mimicked protein, for instance in competition assays since it has been shown that even short peptides (*e.g.*, about 9 amino acids)

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can bind and displace the larger peptides in immunoprecipitation assays. See, e.g., Wilson, et al., (1984) Cell 37:767-778. The anti-peptide antibodies of the invention also are useful for purification of the mimicked protein, for instance, by adsorption chromatography using methods known in the art.

Antigenic epitope-bearing peptides and polypeptides of the invention designed according to the above guidelines preferably contain a sequence of at least seven, more preferably at least nine and most preferably between about 10 to about 50 amino acids (i.e. any integer between 7 and 50) contained within the amino acid sequence of a polypeptide of the invention. However, peptides or polypeptides comprising a larger portion of an amino acid sequence of a polypeptide of the invention, containing about 50 to about 100 amino acids, or any length up to and including the entire amino acid sequence of a polypeptide of the invention, also are considered epitope-bearing peptides or polypeptides of the invention and also are useful for inducing antibodies that react with the mimicked protein. Preferably, the amino acid sequence of the epitope-bearing peptide is selected to provide substantial solubility in aqueous solvents (i.e., the sequence includes relatively hydrophilic residues and highly hydrophobic sequences are preferably avoided); and sequences containing proline residues are particularly preferred.

The epitope-bearing peptides and polypeptides of the present invention may be produced by any conventional means for making peptides or polypeptides including recombinant means using nucleic acid molecules of the invention. For instance, an epitope-bearing amino acid sequence of the present invention may be fused to a larger polypeptide which acts as a carrier during recombinant production and purification, as well as during immunization to produce anti-peptide antibodies. Epitope-bearing peptides also may be synthesized using known methods of chemical synthesis. For instance, Houghten has described a simple method for synthesis of large numbers of peptides, such as 10-20 mg of 248 different 13 residue peptides representing single amino acid variants of a segment of the HA1 polypeptide which were prepared and characterized (by ELISA-type binding studies) in less than four weeks (Houghten, R. A. Proc. Natl. Acad. Sci. USA 82:5131-5135 (1985)). This "Simultaneous Multiple Peptide Synthesis (SMPS)" process is further described in U.S. Patent No. 4,631,211 to Houghten and coworkers (1986). In this procedure the individual resins for the solid-phase synthesis of various peptides are contained in separate solvent-permeable packets, enabling the optimal use of the many identical repetitive steps involved in solid-phase methods. A completely manual procedure allows 500-1000 or more syntheses to be conducted simultaneously (Houghten et al. (1985) Proc. Natl. Acad. Sci. 82:5131-5135 at 5134.

Epitope-bearing peptides and polypeptides of the invention are used to induce antibodies according to methods well known in the art. See, e.g., Sutcliffe, et al., supra;; Wilson, et al., supra;; and Bittle, et al. (1985) J. Gen. Virol. 66:2347-2354. Generally, animals may be immunized with free peptide; however, anti-peptide antibody titer may be boosted by coupling of the peptide to a macromolecular carrier, such as keyhole limpet hemacyanin (KLH) or tetanus toxoid. For instance, peptides containing cysteine may be coupled to carrier using a linker such

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as m-maleimidobenzoyl-N-hydroxysuccinimide ester (MBS), while other peptides may be coupled to carrier using a more general linking agent such as glutaraldehyde. Animals such as rabbits, rats and mice are immunized with either free or carrier-coupled peptides, for instance, by intraperitoneal and/or intradermal injection of emulsions containing about 100 µg peptide or carrier protein and Freund's adjuvant. Several booster injections may be needed, for instance, at intervals of about two weeks, to provide a useful titer of anti-peptide antibody which can be detected, for example, by ELISA assay using free peptide adsorbed to a solid surface. The titer of anti-peptide antibodies in serum from an immunized animal may be increased by selection of anti-peptide antibodies, for instance, by adsorption to the peptide on a solid support and elution of the selected antibodies according to methods well known in the art.

Immunogenic epitope-bearing peptides of the invention, i.e., those parts of a protein that elicit an antibody response when the whole protein is the immunogen, are identified according to methods known in the art. For instance, Geysen, et al., supra, discloses a procedure for rapid concurrent synthesis on solid supports of hundreds of peptides of sufficient purity to react in an ELISA. Interaction of synthesized peptides with antibodies is then easily detected without removing them from the support. In this manner a peptide bearing an immunogenic epitope of a desired protein may be identified routinely by one of ordinary skill in the art. For instance, the immunologically important epitope in the coat protein of foot-and-mouth disease virus was located by Geysen et al. supra with a resolution of seven amino acids by synthesis of an overlapping set of all 208 possible hexapeptides covering the entire 213 amino acid sequence of the protein. Then, a complete replacement set of peptides in which all 20 amino acids were substituted in turn at every position within the epitope were synthesized, and the particular amino acids conferring specificity for the reaction with antibody were determined. Thus, peptide analogs of the epitope-bearing peptides of the invention can be made routinely by this method. U.S. Patent No. 4,708,781 to Geysen (1987) further describes this method of identifying a peptide bearing an immunogenic epitope of a desired protein.

Further still, U.S. Patent No. 5,194,392, to Geysen (1990), describes a general method of detecting or determining the sequence of monomers (amino acids or other compounds) which is a topological equivalent of the epitope (*i.e.*, a "mimotope") which is complementary to a particular paratope (antigen binding site) of an antibody of interest. More generally, U.S. Patent No. 4,433,092, also to Geysen (1989), describes a method of detecting or determining a sequence of monomers which is a topographical equivalent of a ligand which is complementary to the ligand binding site of a particular receptor of interest. Similarly, U.S. Patent No. 5,480,971 to Houghten, R. A. *et al.* (1996) discloses linear C₁-C₇-alkyl peralkylated oligopeptides and sets and libraries of such peptides, as well as methods for using such oligopeptide sets and libraries for determining the sequence of a peralkylated oligopeptide that preferentially binds to an acceptor molecule of interest. Thus, non-peptide analogs of the epitope-bearing peptides of the invention also can be made routinely by these methods. The entire disclosure of each document cited in this section on "Polypeptides and Fragments" is

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hereby incorporated herein by reference.

As one of skill in the art will appreciate, the polypeptides of the present invention and the epitope-bearing fragments thereof described above can be combined with parts of the constant domain of immunoglobulins (IgG), resulting in chimeric polypeptides. These fusion proteins facilitate purification and show an increased half-life *in vivo*. This has been shown, *e.g.*, for chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. (EPA 0,394,827; Traunecker et al. (1988) Nature 331:84-86. Fusion proteins that have a disulfide-linked dimeric structure due to the IgG part can also be more efficient in binding and neutralizing other molecules than a monomeric *B. burgdorferi* polypeptide or fragment thereof alone. *See* Fountoulakis et al. (1995) J. Biochem. 270:3958-3964. Nucleic acids encoding the above epitopes of *B. burgdorferi* polypeptides can also be recombined with a gene of interest as an epitope tag to aid in detection and purification of the expressed polypeptide.

4. Diagnostic Assays and Kits

The present invention further relates to methods for assaying Borrelia infection in an animal by detecting the expression of genes encoding Borrelia polypeptides of the present invention. The methods comprise analyzing tissue or body fluid from the animal for *Borrelia*-specific antibodies, nucleic acids, or proteins. Analysis of nucleic acid specific to *Borrelia* is assayed by PCR or hybridization techniques using nucleic acid sequences of the present invention as either hybridization probes or primers. *See, e.g.,* Sambrook et al. Molecular cloning: A Laboratory Manual (Cold Spring Harbor Laboratory Press, 2nd ed., 1989, page 54 reference); Eremeeva et al. (1994) J. Clin. Microbiol. 32:803-810 (describing differentiation among spotted fever group *Rickettsiae* species by analysis of restriction fragment length polymorphism of PCR-amplified DNA) and Chen et al. 1994 J. Clin. Microbiol. 32:589-595 (detecting *B burgdorferi* nucleic acids *via* PCR).

Where diagnosis of a disease state related to infection with *Borrelia* has already been made, the present invention is useful for monitoring progression or regression of the disease state whereby patients exhibiting enhanced *Borrelia* gene expression will experience a worse clinical outcome relative to patients expressing these gene(s) at a lower level.

By "biological sample" is intended any biological sample obtained from an animal, cell line, tissue culture, or other source which contains *Borrelia* polypeptide, mRNA, or DNA. Biological samples include body fluids (such as saliva, blood, plasma, urine, mucus, synovial fluid, etc.) tissues (such as muscle, skin, and cartilage) and any other biological source suspected of containing *Borrelia* polypeptides or nucleic acids. Methods for obtaining biological samples such as tissue are well known in the art.

The present invention is useful for detecting diseases related to *Borrelia* infections in animals. Preferred animals include monkeys, apes, cats, dogs, birds, cows, pigs, mice, horses, rabbits and humans. Particularly preferred are humans.

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Total RNA can be isolated from a biological sample using any suitable technique such as the single-step guanidinium-thiocyanate-phenol-chloroform method described in Chomczynski et al. (1987) Anal. Biochem. 162:156-159. mRNA encoding *Borrelia* polypeptides having sufficient homology to the nucleic acid sequences identified in SEQ ID NOS:1-155 to allow for hybridization between complementary sequences are then assayed using any appropriate method. These include Northern blot analysis, S1 nuclease mapping, the polymerase chain reaction (PCR), reverse transcription in combination with the polymerase chain reaction (RT-PCR), and reverse transcription in combination with the ligase chain reaction (RT-LCR).

Northern blot analysis can be performed as described in Harada et al. (1990) Cell 63:303-312. Briefly, total RNA is prepared from a biological sample as described above. For the Northern blot, the RNA is denatured in an appropriate buffer (such as glyoxal/dimethyl sulfoxide/sodium phosphate buffer), subjected to agarose gel electrophoresis, and transferred onto a nitrocellulose filter. After the RNAs have been linked to the filter by a UV linker, the filter is prehybridized in a solution containing formamide, SSC, Denhardt's solution, denatured salmon sperm, SDS, and sodium phosphate buffer. A *B. burgdorferi* polynucleotide sequence shown in SEQ ID NOS:1-155 labeled according to any appropriate method (such as the ³²P-multiprimed DNA labeling system (Amersham)) is used as probe. After hybridization overnight, the filter is washed and exposed to x-ray film. DNA for use as probe according to the present invention is described in the sections above and will preferably at least 15 nucleotides in length.

S1 mapping can be performed as described in Fujita et al. (1987) Cell 49:357-367. To prepare probe DNA for use in S1 mapping, the sense strand of an above-described *B. burgdorferi* DNA sequence of the present invention is used as a template to synthesize labeled antisense DNA. The antisense DNA can then be digested using an appropriate restriction endonuclease to generate further DNA probes of a desired length. Such antisense probes are useful for visualizing protected bands corresponding to the target mRNA (*i.e.*, mRNA encoding *Borrelia* polypeptides).

Levels of mRNA encoding *Borrelia* polypeptides are assayed, for *e.g.*, using the RT-PCR method described in Makino et al. (1990) Technique 2:295-301. By this method, the radioactivities of the "amplicons" in the polyacrylamide gel bands are linearly related to the initial concentration of the target mRNA. Briefly, this method involves adding total RNA isolated from a biological sample in a reaction mixture containing a RT primer and appropriate buffer. After incubating for primer annealing, the mixture can be supplemented with a RT buffer, dNTPs, DTT, RNase inhibitor and reverse transcriptase. After incubation to achieve reverse transcription of the RNA, the RT products are then subject to PCR using labeled primers. Alternatively, rather than labeling the primers, a labeled dNTP can be included in the PCR reaction mixture. PCR amplification can be performed in a DNA thermal cycler according to conventional techniques. After a suitable number of rounds to achieve amplification, the PCR reaction mixture is electrophoresed on a polyacrylamide gel. After drying the gel, the radioactivity of the appropriate

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bands (corresponding to the mRNA encoding the *Borrelia* polypeptides of the present invention) are quantified using an imaging analyzer. RT and PCR reaction ingredients and conditions, reagent and gel concentrations, and labeling methods are well known in the art. Variations on the RT-PCR method will be apparent to the skilled artisan. Other PCR methods that can detect the nucleic acid of the present invention can be found in PCR PRIMER: A LABORATORY MANUAL (C.W. Dieffenbach et al. eds., Cold Spring Harbor Lab Press, 1995).

The polynucleotides of the present invention, including both DNA and RNA, may be used to detect polynucleotides of the present invention or Borrelia species including B. burgdorferi using bio chip technology. The present invention includes both high density chip arrays (>1000 oligonucleotides per cm²) and low density chip arrays (<1000 oligonucleotides per cm²). Bio chips comprising arrays of polynucleotides of the present invention may be used to detect Borrelia species, including B. burgdorferi, in biological and environmental samples and to diagnose an animal, including humans, with an B. burgdorferi or other Borrelia infection. The bio chips of the present invention may comprise polynucleotide sequences of other pathogens including bacteria, viral, parasitic, and fungal polynucleotide sequences, in addition to the polynucleotide sequences of the present invention, for use in rapid diffenertial pathogenic detection and diagnosis. The bio chips can also be used to monitor an B. burgdorferi or other Borrelia infections and to monitor the genetic changes (deletions, insertions, mismatches, etc.) in response to drug therapy in the clinic and drug development in the laboratory. The bio chip technology comprising arrays of polynucleotides of the present invention may also be used to simultaneously monitor the expression of a multiplicity of genes, including those of the present invention. The polynucleotides used to comprise a selected array may be specified in the same manner as for the fragements, i.e, by their 5' and 3' positions or length in contigious base pairs and include from. Methods and particular uses of the polynucleotides of the present invention to detect Borrelia species, including B. burgdorferi, using bio chip technology include those known in the art and those of: U.S. Patent Nos. 5510270, 5545531, 5445934, 5677195, 5532128, 5556752, 5527681, 5451683, 5424186, 5607646, 5658732 and World Patent Nos. WO/9710365, WO/9511995, WO/9743447, WO/9535505, each incorporated herein in their entireties.

Biosensors using the polynucleotides of the present invention may also be used to detect, diagnose, and monitor *B. burgdorferi* or other Borrelia species and infections thereof. Biosensors using the polynucleotides of the present invention may also be used to detect particular polynucleotides of the present invention. Biosensors using the polynucleotides of the present invention may also be used to monitor the genetic changes (deletions, insertions, mismatches, etc.) in response to drug therapy in the clinic and drug development in the laboratory. Methods and particular uses of the polynucleotides of the present invention to detect Borrelia species, including *B. burgdorferi*, using biosenors include those known in the art and those of: U.S. Patent Nos 5721102, 5658732, 5631170, and World Patent Nos. WO97/35011, WO/9720203, each incorporated herein in their entireties.

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Thus, the present invention includes both bio chips and biosensors comprising polynucleotides of the present invention and methods of their use.

Assaying *Borrelia* polypeptide levels in a biological sample can occur using any art-known method, such as antibody-based techniques. For example, *Borrelia* polypeptide expression in tissues can be studied with classical immunohistological methods. In these, the specific recognition is provided by the primary antibody (polyclonal or monoclonal) but the secondary detection system can utilize fluorescent, enzyme, or other conjugated secondary antibodies. As a result, an immunohistological staining of tissue section for pathological examination is obtained. Tissues can also be extracted, *e.g.*, with urea and neutral detergent, for the liberation of *Borrelia* polypeptides for Western-blot or dot/slot assay. *See, e.g.*, Jalkanen, M. et al. (1985) J. Cell. Biol. 101:976-985; Jalkanen, M. et al. (1987) J. Cell . Biol. 105:3087-3096. In this technique, which is based on the use of cationic solid phases, quantitation of a *Borrelia* polypeptide can be accomplished using an isolated *Borrelia* polypeptide as a standard. This technique can also be applied to body fluids.

Other antibody-based methods useful for detecting *Borrelia* polypeptide gene expression include immunoassays, such as the ELISA and the radioimmunoassay (RIA). For example, a *Borrelia* polypeptide-specific monoclonal antibodies can be used both as an immunoabsorbent and as an enzyme-labeled probe to detect and quantify a *Borrelia* polypeptide. The amount of a *Borrelia* polypeptide present in the sample can be calculated by reference to the amount present in a standard preparation using a linear regression computer algorithm. Such an ELISA is described in Iacobelli et al. (1988) Breast Cancer Research and Treatment 11:19-30. In another ELISA assay, two distinct specific monoclonal antibodies can be used to detect *Borrelia* polypeptides in a body fluid. In this assay, one of the antibodies is used as the immunoabsorbent and the other as the enzyme-labeled probe.

The above techniques may be conducted essentially as a "one-step" or "two-step" assay. The "one-step" assay involves contacting the *Borrelia* polypeptide with immobilized antibody and, without washing, contacting the mixture with the labeled antibody. The "two-step" assay involves washing before contacting the mixture with the labeled antibody. Other conventional methods may also be employed as suitable. It is usually desirable to immobilize one component of the assay system on a support, thereby allowing other components of the system to be brought into contact with the component and readily removed from the sample. Variations of the above and other immunological methods included in the present invention can also be found in Harlow et al., ANTIBODIES: A LABORATORY MANUAL, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988).

Suitable enzyme labels include, for example, those from the oxidase group, which catalyze the production of hydrogen peroxide by reacting with substrate. Glucose oxidase is particularly preferred as it has good stability and its substrate (glucose) is readily available. Activity of an oxidase label may be assayed by measuring the concentration of hydrogen peroxide formed by the enzyme-labeled antibody/substrate reaction. Besides enzymes, other suitable

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labels include radioisotopes, such as iodine (¹²⁵I, ¹²¹I), carbon (¹⁴C), sulphur (³⁵S), tritium (³H), indium (¹¹²In), and technetium (^{99m}Tc), and fluorescent labels, such as fluorescein and rhodamine, and biotin.

Further suitable labels for the *Borrelia* polypeptide-specific antibodies of the present invention are provided below. Examples of suitable enzyme labels include malate dehydrogenase, Borrelia nuclease, delta-5-steroid isomerase, yeast-alcohol dehydrogenase, alpha-glycerol phosphate dehydrogenase, triose phosphate isomerase, peroxidase, alkaline phosphatase, asparaginase, glucose oxidase, beta-galactosidase, ribonuclease, urease, catalase, glucose-6-phosphate dehydrogenase, glucoamylase, and acetylcholine esterase.

Examples of suitable radioisotopic labels include ³H, ¹¹¹In, ¹²⁵I, ¹³¹I, ³²P, ³⁵S, ¹⁴C, ⁵¹Cr, ⁵⁷To, ⁵⁸Co, ⁵⁹Fe, ⁷⁵Se, ¹⁵²Eu, ⁹⁰Y, ⁶⁷Cu, ²¹⁷Ci, ²¹¹At, ²¹²Pb, ⁴⁷Sc, ¹⁰⁹Pd, etc. ¹¹¹In is a preferred isotope where *in vivo* imaging is used since its avoids the problem of dehalogenation of the ¹²⁵I or ¹³¹I-labeled monoclonal antibody by the liver. In addition, this radionucleotide has a more favorable gamma emission energy for imaging. *See, e.g.*, Perkins et al. (1985) Eur. J. Nucl.

Med. 10:296-301; Carasquillo et al. (1987) J. Nucl. Med. 28:281-287. For example, ¹¹¹In coupled to monoclonal antibodies with 1-(P-isothiocyanatobenzyl)-DPTA has shown little uptake in non-tumors tissues, particularly the liver, and therefore enhances specificity of tumor localization. See, Esteban et al. (1987) J. Nucl. Med. 28:861-870.

Examples of suitable non-radioactive isotopic labels include ¹⁵⁷Gd, ⁵⁵Mn, ¹⁶²Dy, ⁵²Tr, and ⁵⁶Fe.

Examples of suitable fluorescent labels include an ¹⁵²Eu label, a fluorescein label, an isothiocyanate label, a rhodamine label, a phycocrythrin label, a phycocyanin label, an allophycocyanin label, an o-phthaldehyde label, and a fluorescamine label.

Examples of suitable toxin labels include, *Pseudomonas* toxin, diphtheria toxin, ricin, and cholera toxin.

Examples of chemiluminescent labels include a luminal label, an isoluminal label, an aromatic acridinium ester label, an imidazole label, an acridinium salt label, an oxalate ester label, a luciferin label, a luciferase label, and an aequorin label.

Examples of nuclear magnetic resonance contrasting agents include heavy metal nuclei such as Gd, Mn, and iron.

Typical techniques for binding the above-described labels to antibodies are provided by Kennedy et al. (1976) Clin. Chim. Acta 70:1-31, and Schurs et al. (1977) Clin. Chim. Acta 81:1-40. Coupling techniques mentioned in the latter are the glutaraldehyde method, the periodate method, the dimaleimide method, the m-maleimidobenzyl-N-hydroxy-succinimide ester method, all of which methods are incorporated by reference herein.

In a related aspect, the invention includes a diagnostic kit for use in screening serum containing antibodies specific against *B. burgdorferi* infection. Such a kit may include an isolated *B. burgdorferi* antigen comprising an epitope which is specifically immunoreactive with at least one anti-*B. burgdorferi* antibody. Such a kit also includes means for detecting the

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binding of said antibody to the antigen. In specific embodiments, the kit may include a recombinantly produced or chemically synthesized peptide or polypeptide antigen. The peptide or polypeptide antigen may be attached to a solid support.

In a more specific embodiment, the detecting means of the above-described kit includes a solid support to which said peptide or polypeptide antigen is attached. Such a kit may also include a non-attached reporter-labeled anti-human antibody. In this embodiment, binding of the antibody to the *B. burgdorferi* antigen can be detected by binding of the reporter labeled antibody to the anti-*B. burgdorferi* polypeptide antibody.

In a related aspect, the invention includes a method of detecting *B. burgdorferi* infection in a subject. This detection method includes reacting a body fluid, preferably serum, from the subject with an isolated *B. burgdorferi* antigen, and examining the antigen for the presence of bound antibody. In a specific embodiment, the method includes a polypeptide antigen attached to a solid support, and serum is reacted with the support. Subsequently, the support is reacted with a reporter-labeled anti-human antibody. The support is then examined for the presence of reporter-labeled antibody.

The solid surface reagent employed in the above assays and kits is prepared by known techniques for attaching protein material to solid support material, such as polymeric beads, dip sticks, 96-well plates or filter material. These attachment methods generally include non-specific adsorption of the protein to the support or covalent attachment of the protein, typically through a free amine group, to a chemically reactive group on the solid support, such as an activated carboxyl, hydroxyl, or aldehyde group. Alternatively, streptavidin coated plates can be used in conjunction with biotinylated antigen(s).

The polypeptides and antibodies of the present invention, including fragments thereof, may be used to detect Borrelia species including *B. burgdorferi* using bio chip and biosensor technology. Bio chip and biosensors of the present invention may comprise the polypeptides of the present invention to detect antibodies, which specifically recognize Borrelia species, including *B. burgdorferi*. Bio chip and biosensors of the present invention may also comprise antibodies which specifically recognize the polypeptides of the present invention to detect Borrelia species, including *B. burgdorferi* or specific polypeptides of the present invention. Bio chips or biosensors comprising polypeptides or antibodies of the present invention may be used to detect Borrelia species, including *B. burgdorferi*, in biological and environmental samples and to diagnose an animal, including humans, with an *B. burgdorferi* or other Borrelia infection. Thus, the present invention includes both bio chips and biosensors comprising polypeptides or antibodies of the present invention and methods of their use.

The bio chips of the present invention may further comprise polypeptide sequences of other pathogens including bacteria, viral, parasitic, and fungal polypeptide sequences, in addition to the polypeptide sequences of the present invention, for use in rapid differential pathogenic detection and diagnosis. The bio chips of the present invention may further comprise antibodies or fragements thereof specific for other pathogens including bacteria, viral, parasitic, and fungal

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polypeptide sequences, in addition to the antibodies or fragements thereof of the present invention, for use in rapid diffenertial pathogenic detection and diagnosis. The bio chips and biosensors of the present invention may also be used to monitor an B. burgdorferi or other Borrelia infection and to monitor the genetic changes (amio acid deletions, insertions, substitutions, etc.) in response to drug therapy in the clinic and drug development in the 5 laboratory. The bio chip and biosensors comprising polypeptides or antibodies of the present invention may also be used to simultaneously monitor the expression of a multiplicity of polypeptides, including those of the present invention. The polypeptides used to comprise a bio chip or biosensor of the present invention may be specified in the same manner as for the 10 fragements, i.e, by their N-terminal and C-terminal positions or length in contigious amino acid residue. Methods and particular uses of the polypeptides and antibodies of the present invention to detect Borrelia species, including B. burgdorferi, or specific polypeptides using bio chip and biosensor technology include those known in the art, those of the U.S. Patent Nos. and World Patent Nos. listed above for bio chips and biosensors using polynucleotides of the present invention, and those of: U.S. Patent Nos. 5658732, 5135852, 5567301, 5677196, 5690894 15 and World Patent Nos. WO9729366, WO9612957, each incorporated herein in their entireties.

5. Screening Assay for Binding Agents

Using the isolated proteins of the present invention, the present invention further provides methods of obtaining and identifying agents which bind to a protein encoded by one of the ORFs of the present invention or to one of the fragments and the *Borrelia burgdorferi* fragment and contigs herein described.

In general, such methods comprise steps of:

- (a) contacting an agent with an isolated protein encoded by one of the ORFs of the present invention, or an isolated fragment of the *Borrelia burgdorferi* genome; and
 - (b) determining whether the agent binds to said protein or said fragment.

The agents screened in the above assay can be, but are not limited to, peptides, carbohydrates, vitamin derivatives, or other pharmaceutical agents. The agents can be selected and screened at random or rationally selected or designed using protein modeling techniques.

For random screening, agents such as peptides, carbohydrates, pharmaceutical agents and the like are selected at random and are assayed for their ability to bind to the protein encoded by the ORF of the present invention.

Alternatively, agents may be rationally selected or designed. As used herein, an agent is said to be "rationally selected or designed" when the agent is chosen based on the configuration of the particular protein. For example, one skilled in the art can readily adapt currently available procedures to generate peptides, pharmaceutical agents and the like capable of binding to a specific peptide sequence in order to generate rationally designed antipeptide peptides, for example see Hurby *et al.*, "Application of Synthetic Peptides: Antisense Peptides," in *Synthetic*

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Peptides, A User's Guide, W. H. Freeman, NY (1992), pp. 289-307, and Kaspczak et al., Biochemistry 28:9230-8 (1989), or pharmaceutical agents, or the like.

In addition to the foregoing, one class of agents of the present invention, as broadly described, can be used to control gene expression through binding to one of the ORFs or EMFs of the present invention. As described above, such agents can be randomly screened or rationally designed/selected. Targeting the ORF or EMF allows a skilled artisan to design sequence specific or element specific agents, modulating the expression of either a single ORF or multiple ORFs which rely on the same EMF for expression control.

One class of DNA binding agents are agents which contain base residues which hybridize or form a triple helix by binding to DNA or RNA. Such agents can be based on the classic phosphodiester, ribonucleic acid backbone, or can be a variety of sulfhydryl or polymeric derivatives which have base attachment capacity.

Agents suitable for use in these methods usually contain 20 to 40 bases and are designed to be complementary to a region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988)). Triple helix- formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques have been demonstrated to be effective in model systems. Information contained in the sequences of the present invention can be used to design antisense and triple helix-forming oligonucleotides, and other DNA binding agents.

6. Pharmaceutical Compositions and Vaccines

The present invention further provides pharmaceutical agents which can be used to modulate the growth or pathogenicity of *Borrelia burgdorferi*, or another related organism, *in vivo* or *in vitro*. As used herein, a "pharmaceutical agent" is defined as a composition of matter which can be formulated using known techniques to provide a pharmaceutical compositions. As used herein, the "pharmaceutical agents of the present invention" refers the pharmaceutical agents which are derived from the proteins encoded by the ORFs of the present invention or are agents which are identified using the herein described assays.

As used herein, a pharmaceutical agent is said to "modulate the growth pathogenicity of Borrelia burgdorferi or a related organism, in vivo or in vitro," when the agent reduces the rate of growth, rate of division, or viability of the organism in question. The pharmaceutical agents of the present invention can modulate the growth or pathogenicity of an organism in many fashions, although an understanding of the underlying mechanism of action is not needed to practice the use of the pharmaceutical agents of the present invention. Some agents will modulate the growth by binding to an important protein thus blocking the biological activity of the protein, while other agents may bind to a component of the outer surface of the organism blocking attachment or

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rendering the organism more prone to act the bodies nature immune system. Alternatively, the agent may comprise a protein encoded by one of the ORFs of the present invention and serve as a vaccine. The development and use of a vaccine based on outer membrane components are well known in the art.

As used herein, a "related organism" is a broad term which refers to any organism whose growth can be modulated by one of the pharmaceutical agents of the present invention. In general, such an organism will contain a homolog of the protein which is the target of the pharmaceutical agent or the protein used as a vaccine. As such, related organisms do not need to be bacterial but may be fungal or viral pathogens.

The pharmaceutical agents and compositions of the present invention may be administered in a convenient manner, such as by the oral, topical, intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal or intradermal routes. The pharmaceutical compositions are administered in an amount which is effective for treating and/or prophylaxis of the specific indication. In general, they are administered in an amount of at least about 1 mg/kg body weight and in most cases they will be administered in an amount not in excess of about 1 g/kg body weight per day. In most cases, the dosage is from about 0.1 mg/kg to about 10 g/kg body weight daily, taking into account the routes of administration, symptoms, etc.

The agents of the present invention can be used in native form or can be modified to form a chemical derivative. As used herein, a molecule is said to be a "chemical derivative" of another molecule when it contains additional chemical moieties not normally a part of the molecule. Such moieties may improve the molecule's solubility, absorption, biological half life, *etc*. The moieties may alternatively decrease the toxicity of the molecule, eliminate or attenuate any undesirable side effect of the molecule, *etc*. Moieties capable of mediating such effects are disclosed in, among other sources, REMINGTON'S PHARMACEUTICAL SCIENCES (1980) cited elsewhere herein.

For example, such moieties may change an immunological character of the functional derivative, such as affinity for a given antibody. Such changes in immunomodulation activity are measured by the appropriate assay, such as a competitive type immunoassay. Modifications of such protein properties as redox or thermal stability, biological half-life, hydrophobicity, susceptibility to proteolytic degradation or the tendency to aggregate with carriers or into multimers also may be effected in this way and can be assayed by methods well known to the skilled artisan.

The therapeutic effects of the agents of the present invention may be obtained by providing the agent to a patient by any suitable means (e.g., inhalation, intravenously, intramuscularly, subcutaneously, enterally, or parenterally). It is preferred to administer the agent of the present invention so as to achieve an effective concentration within the blood or tissue in which the growth of the organism is to be controlled. To achieve an effective blood concentration, the preferred method is to administer the agent by injection. The administration may be by continuous infusion, or by single or multiple injections.

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In providing a patient with one of the agents of the present invention, the dosage of the administered agent will vary depending upon such factors as the patient's age, weight, height, sex, general medical condition, previous medical history, etc. In general, it is desirable to provide the recipient with a dosage of agent which is in the range of from about 1 pg/kg to 10 mg/kg (body weight of patient), although a lower or higher dosage may be administered. The therapeutically effective dose can be lowered by using combinations of the agents of the present invention or another agent.

As used herein, two or more compounds or agents are said to be administered "in combination" with each other when either (1) the physiological effects of each compound, or (2) the serum concentrations of each compound can be measured at the same time. The composition of the present invention can be administered concurrently with, prior to, or following the administration of the other agent.

The agents of the present invention are intended to be provided to recipient subjects in an amount sufficient to decrease the rate of growth (as defined above) of the target organism.

The administration of the agent(s) of the invention may be for either a "prophylactic" or "therapeutic" purpose. When provided prophylactically, the agent(s) are provided in advance of any symptoms indicative of the organisms growth. The prophylactic administration of the agent(s) serves to prevent, attenuate, or decrease the rate of onset of any subsequent infection. When provided therapeutically, the agent(s) are provided at (or shortly after) the onset of an indication of infection. The therapeutic administration of the compound(s) serves to attenuate the pathological symptoms of the infection and to increase the rate of recovery.

The agents of the present invention are administered to a subject, such as a mammal, or a patient, in a pharmaceutically acceptable form and in a therapeutically effective concentration. A composition is said to be "pharmacologically acceptable" if its administration can be tolerated by a recipient patient. Such an agent is said to be administered in a "therapeutically effective amount" if the amount administered is physiologically significant. An agent is physiologically significant if its presence results in a detectable change in the physiology of a recipient patient.

The agents of the present invention can be formulated according to known methods to prepare pharmaceutically useful compositions, whereby these materials, or their functional derivatives, are combined in a mixture with a pharmaceutically acceptable carrier vehicle. Suitable vehicles and their formulation, inclusive of other human proteins, *e.g.*, human serum albumin, are described, for example, in REMINGTON'S PHARMACEUTICAL SCIENCES, 16th Ed., Osol, A., Ed., Mack Publishing, Easton PA (1980). In order to form a pharmaceutically acceptable composition suitable for effective administration, such compositions will contain an effective amount of one or more of the agents of the present invention, together with a suitable amount of carrier vehicle.

Additional pharmaceutical methods may be employed to control the duration of action. Control release preparations may be achieved through the use of polymers to complex or absorb one or more of the agents of the present invention. The controlled delivery may be effectuated by

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a variety of well known techniques, including formulation with macromolecules such as, for example, polyesters, polyamino acids, polyvinyl, pyrrolidone, ethylenevinylacetate, methylcellulose, carboxymethylcellulose, or protamine, sulfate, adjusting the concentration of the macromolecules and the agent in the formulation, and by appropriate use of methods of incorporation, which can be manipulated to effectuate a desired time course of release. Another possible method to control the duration of action by controlled release preparations is to incorporate agents of the present invention into particles of a polymeric material such as polyesters, polyamino acids, hydrogels, poly(lactic acid) or ethylene vinylacetate copolymers. Alternatively, instead of incorporating these agents into polymeric particles, it is possible to entrap these materials in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization with, for example, hydroxymethylcellulose or gelatine-microcapsules and poly(methylmethacylate) microcapsules, respectively, or in colloidal drug delivery systems, for example, liposomes, albumin microspheres, microemulsions, nanoparticles, and nanocapsules or in macroemulsions. Such techniques are disclosed in REMINGTON'S PHARMACEUTICAL SCIENCES (1980).

The invention further provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

In addition, the agents of the present invention may be employed in conjunction with other therapeutic compounds.

7. Shot-Gun Approach to Megabase DNA Sequencing

The present invention further demonstrates that a large sequence can be sequenced using a random shotgun approach. This procedure, described in detail in the examples that follow, has eliminated the up front cost of isolating and ordering overlapping or contiguous subclones prior to the start of the sequencing protocols.

Certain aspects of the present invention are described in greater detail in the examples that follow. The examples are provided by way of illustration. Other aspects and embodiments of the present invention are contemplated by the inventors, as will be clear to those of skill in the art from reading the present disclosure.

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ILLUSTRATIVE EXAMPLES

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1. Shotgun Sequencing Probability Analysis

The overall strategy for a shotgun approach to whole genome sequencing follows from the Lander and Waterman (Landerman and Waterman, *Genomics* 2:231 (1988)) application of the equation for the Poisson distribution. According to this treatment, the probability, P0, that any given base in a sequence of size L, in nucleotides, is not sequenced after a certain amount, n, in nucleotides, of random sequence has been determined can be calculated by the equation P0 = e-m, where m is L/n, the fold coverage. For instance, for a genome of 2.8 Mb, m=1 when 2.8 Mb of sequence has been randomly generated (1X coverage). At that point, P0 = e-1 = 0.37. The probability that any given base has not been sequenced is the same as the probability that any region of the whole sequence L has not been determined and, therefore, is equivalent to the fraction of the whole sequence that has yet to be determined. Thus, at one-fold coverage, approximately 37% of a polynucleotide of size L, in nucleotides has not been sequenced. When 14 Mb of sequence has been generated, coverage is 5X for a 2.8 Mb and the unsequenced fraction drops to .0067 or 0.67%. 5X coverage of a 2.8 Mb sequence can be attained by sequencing approximately 17,000 random clones from both insert ends with an average sequence read length of 410 bp.

Similarly, the total gap length, G, is determined by the equation G = Le-m, and the average gap size, g, follows the equation, g = L/n. Thus, 5X coverage leaves about 240 gaps averaging about 82 bp in size in a sequence of a polynucleotide 2.8 Mb long.

The treatment above is essentially that of Lander and Waterman, *Genomics* 2: 231 (1988).

2. Random Library Construction

In order to approximate the random model described above during actual sequencing, a nearly ideal library of cloned genomic fragments is required. The following library construction procedure was developed to achieve this end.

Borrelia burgdorferi DNA is prepared by phenol extraction. A mixture containing 200 μg DNA in 1.0 ml of 300 mM sodium acetate, 10 mM Tris-HCl, 1 mM Na-EDTA, 50% glycerol is processed through a nebulizer (IPI Medical Products) with a stream of nitrogen adjusted to 35 Kpa for 2 minutes. The sonicated DNA is ethanol precipitated and redissolved in 500 μ l TE buffer.

To create blunt-ends, a 100 μ l aliquot of the resuspended DNA is digested with 5 units of BAL31 nuclease (New England BioLabs) for 10 min at 30°C in 200 μ l BAL31 buffer. The digested DNA is phenol-extracted, ethanol-precipitated, redissolved in 100 μ l TE buffer, and then size-fractionated by electrophoresis through a 1.0% low melting temperature agarose gel. The section containing DNA fragments 1.6-2.0 kb in size is excised from the gel, and the LGT agarose is melted and the resulting solution is extracted with phenol to separate the agarose from the DNA. DNA is ethanol precipitated and redissolved in 20 μ l of TE buffer for ligation to vector.

A two-step ligation procedure is used to produce a plasmid library with 97% inserts, of which >99% were single inserts. The first ligation mixture (50 ul) contains 2 μg of DNA fragments, 2 µg pUC18 DNA (Pharmacia) cut with SmaI and dephosphorylated with bacterial alkaline phosphatase, and 10 units of T4 ligase (GIBCO/BRL) and is incubated at 14°C for 4 hr. The ligation mixture then is phenol extracted and ethanol precipitated, and the precipitated DNA is 5 dissolved in 20 µl TE buffer and electrophoresed on a 1.0% low melting agarose gel. Discrete bands in a ladder are visualized by ethidium bromide-staining and UV illumination and identified by size as insert (I), vector (v), v+I, v+2i, v+3i, etc. The portion of the gel containing v+I DNA is excised and the v+I DNA is recovered and resuspended into 20 μl TE. The v+I DNA then is blunt-ended by T4 polymerase treatment for 5 min. at 37°C in a reaction mixture (50 ul) 10 containing the v+I linears, 500 μM each of the 4 dNTPs, and 9 units of T4 polymerase (New England BioLabs), under recommended buffer conditions. After phenol extraction and ethanol precipitation the repaired v+I linears are dissolved in 20 µl TE. The final ligation to produce circles is carried out in a 50 μ l reaction containing 5 μ l of v+I linears and 5 units of T4 ligase at 14°C overnight. After 10 min. at 70°C the following day, the reaction mixture is stored at -20°C. 15

This two-stage procedure results in a molecularly random collection of single-insert plasmid recombinants with minimal contamination from double-insert chimeras (<1%) or free vector (<3%).

Since deviation from randomness can arise from propagation the DNA in the host, *E. coli* host cells deficient in all recombination and restriction functions (A. Greener, *Strategies 3 (1)*:5 (1990)) are used to prevent rearrangements, deletions, and loss of clones by restriction. Furthermore, transformed cells are plated directly on antibiotic diffusion plates to avoid the usual broth recovery phase which allows multiplication and selection of the most rapidly growing cells.

Plating is carried out as follows. A 100 µl aliquot of Epicurian Coli SURE II 25 Supercompetent Cells (Stratagene 200152) is thawed on ice and transferred to a chilled Falcon 2059 tube on ice. A 1.7 µl aliquot of 1.42 M beta-mercaptoethanol is added to the aliquot of cells to a final concentration of 25 mM. Cells are incubated on ice for 10 min. A 1 μ l aliquot of the final ligation is added to the cells and incubated on ice for 30 min. The cells are heat pulsed for 30 sec. at 42°C and placed back on ice for 2 min. The outgrowth period in liquid culture is eliminated from this protocol in order to minimize the preferential growth of any given 30 transformed cell. Instead the transformation mixture is plated directly on a nutrient rich SOB plate containing a 5 ml bottom layer of SOB agar (5% SOB agar: 20 g tryptone, 5 g yeast extract, 0.5 g NaCl, 1.5% Difco Agar per liter of media). The 5 ml bottom layer is supplemented with 0.4 ml of 50 mg/ml ampicillin per 100 ml SOB agar. The 15 ml top layer of SOB agar is 35 supplemented with 1 ml X-Gal (2%), 1 ml MgCl2 (1 M), and 1 ml MgSO4/100 ml SOB agar. The 15 ml top layer is poured just prior to plating. Our titer is approximately 100 colonies/10 µl aliquot of transformation.

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All colonies are picked for template preparation regardless of size. Thus, only clones lost due to "poison" DNA or deleterious gene products are deleted from the library, resulting in a slight increase in gap number over that expected.

3. Random DNA Sequencing

High quality double stranded DNA plasmid templates are prepared using a "boiling bead" method developed in collaboration with Advanced Genetic Technology Corp. (Gaithersburg, MD) (Adams et al., Science 252:1651 (1991); Adams et al., Nature 355:632 (1992)). Plasmid preparation is performed in a 96-well format for all stages of DNA preparation from bacterial growth through final DNA purification. Template concentration is determined using Hoechst Dye and a Millipore Cytofluor. DNA concentrations are not adjusted, but low-yielding templates are identified where possible and not sequenced.

Templates are also prepared from two Borrelia burgdorferi lambda genomic libraries. An amplified library is constructed in the vector Lambda GEM-12 (Promega) and an unamplified library is constructed in Lambda DASH II (Stratagene). In particular, for the unamplified lambda library, Borrelia burgdorferi DNA (> 100 kb) is partially digested in a reaction mixture (200 ul) containing 50 µg DNA, 1X Sau3AI buffer, 20 units Sau3AI for 6 min. at 23°C. The digested DNA was phenol-extracted and electrophoresed on a 0.5% low melting agarose gel at 2V/cm for 7 hours. Fragments from 15 to 25 kb are excised and recovered in a final volume of 6 ul. One μl of fragments is used with 1 μl of DASHII vector (Stratagene) in the recommended ligation reaction. One µl of the ligation mixture is used per packaging reaction following the recommended protocol with the Gigapack II XL Packaging Extract (Stratagene, #227711). Phage are plated directly without amplification from the packaging mixture (after dilution with $500\,\mu l$ of recommended SM buffer and chloroform treatment). Yield is about 2.5x103 pfu/ul. The amplified library is prepared essentially as above except the lambda GEM-12 vector is used. After packaging, about 3.5x104 pfu are plated on the restrictive NM539 host. The lysate is harvested in 2 ml of SM buffer and stored frozen in 7% dimethylsulfoxide. The phage titer is approximately 1x109 pfu/ml.

Liquid lysates (100 μ l) are prepared from randomly selected plaques (from the unamplified library) and template is prepared by long-range PCR using T7 and T3 vector-specific primers.

Sequencing reactions are carried out on plasmid and/or PCR templates using the AB Catalyst LabStation with Applied Biosystems PRISM Ready Reaction Dye Primer Cycle Sequencing Kits for the M13 forward (M13-21) and the M13 reverse (M13RP1) primers (Adams et al., Nature 368:474 (1994)). Dye terminator sequencing reactions are carried out on the lambda templates on a Perkin-Elmer 9600 Thermocycler using the Applied Biosystems Ready Reaction Dye Terminator Cycle Sequencing kits. T7 and SP6 primers are used to sequence the ends of the inserts from the Lambda GEM-12 library and T7 and T3 primers are used to sequence the ends of the inserts from the Lambda DASH II library. Sequencing reactions are performed

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by eight individuals using an average of fourteen AB 373 DNA Sequencers per day. All sequencing reactions are analyzed using the Stretch modification of the AB 373, primarily using a 34 cm well-to-read distance. The overall sequencing success rate very approximately is about 85% for M13-21 and M13RP1 sequences and 65% for dye-terminator reactions. The average usable read length is 485 bp for M13-21 sequences, 445bp for M13RP1 sequences, and 375 bp for dye-terminator reactions.

Richards *et al.*, Chapter 28 in AUTOMATED DNA SEQUENCING AND ANALYSIS, M. D. Adams, C. Fields, J. C. Venter, Eds., Academic Press, London, (1994) described the value of using sequence from both ends of sequencing templates to facilitate ordering of contigs in shotgun assembly projects of lambda and cosmid clones. We balance the desirability of bothend sequencing (including the reduced cost of lower total number of templates) against shorter read-lengths for sequencing reactions performed with the M13RP1 (reverse) primer compared to the M13-21 (forward) primer. Approximately one-half of the templates are sequenced from both ends. Random reverse sequencing reactions are done based on successful forward sequencing reactions. Some M13RP1 sequences are obtained in a semi-directed fashion: M13-21: sequences pointing outward at the ends of contigs are chosen for M13RP1 sequencing in an effort to specifically order contigs.

4. Protocol for Automated Cycle Sequencing

The sequencing is carried out using ABI Catalyst robots and AB 373 Automated DNA Sequencers. The Catalyst robot is a publicly available sophisticated pipetting and temperature control robot which has been developed specifically for DNA sequencing reactions. The Catalyst combines pre-aliquoted templates and reaction mixes consisting of deoxy- and dideoxynucleotides, the thermostable Taq DNA polymerase, fluorescently-labelled sequencing primers, and reaction buffer. Reaction mixes and templates are combined in the wells of an aluminum 96-well thermocycling plate. Thirty consecutive cycles of linear amplification (i.e.., one primer synthesis) steps are performed including denaturation, annealing of primer and template, and extension; i.e., DNA synthesis. A heated lid with rubber gaskets on the thermocycling plate prevents evaporation without the need for an oil overlay.

Two sequencing protocols are used: one for dye-labelled primers and a second for dye-labelled dideoxy chain terminators. The shotgun sequencing involves use of four dye-labelled sequencing primers, one for each of the four terminator nucleotide. Each dye-primer is labelled with a different fluorescent dye, permitting the four individual reactions to be combined into one lane of the 373 DNA Sequencer for electrophoresis, detection, and base-calling. ABI currently supplies pre-mixed reaction mixes in bulk packages containing all the necessary non-template reagents for sequencing. Sequencing can be done with both plasmid and PCR- generated templates with both dye-primers and dye- terminators with approximately equal fidelity, although plasmid templates generally give longer usable sequences.

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Thirty-two reactions are loaded per AB373 Sequencer each day, for a total of 960 samples. Electrophoresis is run overnight following the manufacturer's protocols, and the data is collected for twelve hours. Following electrophoresis and fluorescence detection, the ABI 373 performs automatic lane tracking and base-calling. The lane-tracking is confirmed visually. Each sequence electropherogram (or fluorescence lane trace) is inspected visually and assessed for quality. Trailing sequences of low quality are removed and the sequence itself is loaded via software to a Sybase database (archived daily to 8mm tape). Leading vector polylinker sequence is removed automatically by a software program. Average edited lengths of sequences from the standard ABI 373 are around 400 bp and depend mostly on the quality of the template used for the sequencing reaction. ABI 373 Sequencers converted to Stretch Liners provide a longer electrophoresis path prior to fluorescence detection and increase the average number of usable bases to 500-600 bp.

INFORMATICS

1. Data Management

A number of information management systems for a large-scale sequencing lab have been developed. (For review see, for instance, Kerlavage et al., Proceedings of the Twenty-Sixth Annual Hawaii International Conference on System Sciences, IEEE Computer Society Press, Washington D. C., 585 (1993)) The system used to collect and assemble the sequence data was developed using the Sybase relational database management system and was designed to automate data flow wherever possible and to reduce user error. The database stores and correlates all information collected during the entire operation from template preparation to final analysis of the genome. Because the raw output of the ABI 373 Sequencers was based on a Macintosh platform and the data management system chosen was based on a Unix platform, it was necessary to design and implement a variety of multi- user, client-server applications which allow the raw data as well as analysis results to flow seamlessly into the database with a minimum of user effort.

2. Assembly

An assembly engine (TIGR Assembler) developed for the rapid and accurate assembly of thousands of sequence fragments was employed to generate contigs. The TIGR assembler simultaneously clusters and assembles fragments of the genome. In order to obtain the speed necessary to assemble more than 104 fragments, the algorithm builds a hash table of 12 bp oligonucleotide subsequences to generate a list of potential sequence fragment overlaps. The number of potential overlaps for each fragment determines which fragments are likely to fall into repetitive elements. Beginning with a single seed sequence fragment, TIGR Assembler extends the current contig by attempting to add the best matching fragment based on oligonucleotide content. The contig and candidate fragment are aligned using a modified version of the Smith-Waterman algorithm which provides for optimal gapped alignments (Waterman, M. S., Methods

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in Enzymology 164:765 (1988)). The contig is extended by the fragment only if strict criteria for the quality of the match are met. The match criteria include the minimum length of overlap, the maximum length of an unmatched end, and the minimum percentage match. These criteria are automatically lowered by the algorithm in regions of minimal coverage and raised in regions with a possible repetitive element. The number of potential overlaps for each fragment determines which fragments are likely to fall into repetitive elements. Fragments representing the boundaries of repetitive elements and potentially chimeric fragments are often rejected based on partial mismatches at the ends of alignments and excluded from the current contig. TIGR Assembler is designed to take advantage of clone size information coupled with sequencing from both ends of each template. It enforces the constraint that sequence fragments from two ends of the same template point toward one another in the contig and are located within a certain range of base pairs (definable for each clone based on the known clone size range for a given library). The process resulted in 155 contigs as represented by SEQ ID NOs:1-155.

3. Identifying Genes

The predicted coding regions of the *Borrelia burgdorferi* genome were initially defined with the program GeneMark, which finds ORFs using a probabilistic classification technique. The predicted coding region sequences were used in searches against a database of all nucleotide sequences from GenBank (July, 1997), using the BLASTN search method to identify overlaps of 50 or more nucleotides with at least a 95% identity (using default parameters). Those ORFs with nucleotide sequence matches are shown in Table 1. The ORFs without such matches were translated to protein sequences and compared to a non-redundant database of known proteins generated by combining the Swiss-prot, PIR and GenPept databases. ORFs that matched a database protein with BLASTP probability less than or equal to 0.01 are shown in Table 2. The table also lists assigned functions based on the closest match in the databases. ORFs that did not match protein or nucleotide sequences in the databases at these levels are shown in Table 3.

ILLUSTRATIVE APPLICATIONS

1. Production of an Antibody to a Borrelia burgdorferi Protein

Substantially pure protein or polypeptide is isolated from the transfected or transformed cells using any one of the methods known in the art. The protein can also be produced in a recombinant prokaryotic expression system, such as *E. coli*, or can be chemically synthesized. Concentration of protein in the final preparation is adjusted, for example, by concentration on an Amicon filter device, to the level of a few micrograms/ml. Monoclonal or polyclonal antibody to the protein can then be prepared as follows.

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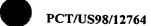
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2. Monoclonal Antibody Production by Hybridoma Fusion

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Monoclonal antibody to epitopes of any of the peptides identified and isolated as described can be prepared from murine hybridomas according to the classical method of Kohler, G. and Milstein, C., *Nature* 256:495 (1975) or modifications of the methods thereof. Briefly, a mouse is repetitively inoculated with a few micrograms of the selected protein over a period of a few weeks. The mouse is then sacrificed, and the antibody producing cells of the spleen isolated. The spleen cells are fused by means of polyethylene glycol with mouse myeloma cells, and the excess unfused cells destroyed by growth of the system on selective media comprising aminopterin (HAT media). The successfully fused cells are diluted and aliquots of the dilution placed in wells of a microtiter plate where growth of the culture is continued. Antibody-producing clones are identified by detection of antibody in the supernatant fluid of the wells by immunoassay procedures, such as ELISA, as originally described by Engvall, E., *Meth. Enzymol.* 70:419 (1980), and modified methods thereof. Selected positive clones can be expanded and their monoclonal antibody product harvested for use. Detailed procedures for monoclonal antibody production are described in Davis, L. *et al.*, *Basic Methods in Molecular Biology*, Elsevier, New York. Section 21-2 (1989).

3. Polyclonal Antibody Production by Immunization

Polyclonal antiserum containing antibodies to heterogenous epitopes of a single protein can be prepared by immunizing suitable animals with the expressed protein described above, which can be unmodified or modified to enhance immunogenicity. Effective polyclonal antibody production is affected by many factors related both to the antigen and the host species. For example, small molecules tend to be less immunogenic than others and may require the use of carriers and adjuvant. Also, host animals vary in response to site of inoculations and dose, with both inadequate or excessive doses of antigen resulting in low titer antisera. Small doses (ng level) of antigen administered at multiple intradermal sites appears to be most reliable. An effective immunization protocol for rabbits can be found in Vaitukaitis, J. et al., J. Clin. Endocrinol. Metab. 33:988-991 (1971).

Booster injections can be given at regular intervals, and antiserum harvested when antibody titer thereof, as determined semi-quantitatively, for example, by double immunodiffusion in agar against known concentrations of the antigen, begins to fall. See, for example, Ouchterlony, O. et al., Chap. 19 in: Handbook of Experimental Immunology, Wier, D., ed, Blackwell (1973). Plateau concentration of antibody is usually in the range of 0. 1 to 0. 2 mg/ml of serum (about 12M). Affinity of the antisera for the antigen is determined by preparing competitive binding curves, as described, for example, by Fisher, D., Chap. 42 in: Manual of Clinical Immunology, second edition, Rose and Friedman, eds., Amer. Soc. For Microbiology, Washington, D. C. (1980)

Antibody preparations prepared according to either protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological

samples; they are also used semi- quantitatively or qualitatively to identify the presence of antigen in a biological sample. In addition, antibodies are useful in various animal models of pneumococcal disease as a means of evaluating the protein used to make the antibody as a potential vaccine target or as a means of evaluating the antibody as a potential immunotherapeutic or immunoprophylactic reagent.

4. Preparation of PCR Primers and Amplification of DNA

Various fragments of the *Borrelia burgdorferi* genome, such as those of Tables 1-6 and SEQ ID NOS: 1-155 can be used, in accordance with the present invention, to prepare PCR primers for a variety of uses. The PCR primers are preferably at least 15 bases, and more preferably at least 18 bases in length. When selecting a primer sequence, it is preferred that the primer pairs have approximately the same G/C ratio, so that melting temperatures are approximately the same. The PCR primers and amplified DNA of this Example find use in the Examples that follow.

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5. Isolation of a Selected DNA Clone From B. burgdorferi

Three approaches are used to isolate a *B. burgdorferi* clone comprising a polynucleotide of the present invention from any *B. burgdorferi* genomic DNA library. The *B. burgdorferi* strain B31PU has been deposited as a convienent source for obtaining a *B. burgdorferi* strain although a wide varity of strains *B. burgdorferi* strains can be used which are known in the art.

B. burgdorferi genomic DNA is prepared using the following method. A 20ml overnight bacterial culture grown in a rich medium (e.g., Trypticase Soy Broth, Brain Heart Infusion broth or Super broth), pelleted, ished two times with TES (30mM Tris-pH 8.0, 25mM EDTA, 50mM NaCl), and resuspended in 5ml high salt TES (2.5M NaCl). Lysostaphin is added to final concentration of approx 50ug/ml and the mixture is rotated slowly 1 hour at 37C to make protoplast cells. The solution is then placed in incubator (or place in a shaking water bath) and warmed to 55C. Five hundred micro liter of 20% sarcosyl in TES (final concentration 2%) is then added to lyse the cells. Next, guanidine HCl is added to a final concentration of 7M (3.69g in 5.5 ml). The mixture is swirled slowly at 55C for 60-90 min (solution should clear). A CsCl gradient is then set up in SW41 ultra clear tubes using 2.0ml 5.7M CsCl and overlaying with 2.85M CsCl. The gradient is carefully overlayed with the DNA-containing GuHCl solution. The gradient is spun at 30,000 rpm, 20C for 24 hr and the lower DNA band is collected. The volume is increased to 5 ml with TE buffer. The DNA is then treated with protease K (10 ug/ml) overnight at 37 C, and precipitated with ethanol. The precipitated DNA is resuspended in a desired buffer.

In the first method, a plasmid is directly isolated by screening a plasmid *B. burgdorferi* genomic DNA library using a polynucleotide probe corresponding to a polynucleotide of the present invention. Particularly, a specific polynucleotide with 30-40 nucleotides is synthesized using an Applied Biosystems DNA synthesizer according to the sequence reported. The

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oligonucleotide is labeled, for instance, with ³²P-γ-ATP using T4 polynucleotide kinase and purified according to routine methods. (*See, e.g.*, Maniatis et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, Cold Spring, NY (1982).) The library is transformed into a suitable host, as indicated above (such as XL-1 Blue (Stratagene)) using techniques known to those of skill in the art. *See, e.g.*, Sambrook et al. MOLECULAR CLONING: A LABORATORY MANUAL (Cold Spring Harbor, N.Y. 2nd ed. 1989); Ausubel et al., CURRENT PROTOCALS IN MOLECULAR BIOLOGY (John Wiley and Sons, N.Y. 1989). The transformants are plated on 1.5% agar plates (containing the appropriate selection agent, e.g., ampicillin) to a density of about 150 transformants (colonies) per plate. These plates are screened using Nylon membranes according to routine methods for bacterial colony screening. *See, e.g.*, Sambrook et al. MOLECULAR CLONING: A LABORATORY MANUAL (Cold Spring Harbor, N.Y. 2nd ed. 1989); Ausubel et al., CURRENT PROTOCALS IN MOLECULAR BIOLOGY (John Wiley and Sons, N.Y. 1989) or other techniques known to those of skill in the art.

Alternatively, two primers of 15-25 nucleotides derived from the 5' and 3' ends of a polynucleotide of SEQ ID NOS:1-155 are synthesized and used to amplify the desired DNA by PCR using a *B. burgdorferi* genomic DNA prep as a template. PCR is carried out under routine conditions, for instance, in 25 µl of reaction mixture with 0.5 ug of the above DNA template. A convenient reaction mixture is 1.5-5 mM MgCl₂, 0.01% (w/v) gelatin, 20 µM each of dATP, dCTP, dGTP, dTTP, 25 pmol of each primer and 0.25 Unit of Taq polymerase. Thirty five cycles of PCR (denaturation at 94°C for 1 min; annealing at 55°C for 1 min; elongation at 72°C for 1 min) are performed with a Perkin-Elmer Cetus automated thermal cycler. The amplified product is analyzed by agarose gel electrophoresis and the DNA band with expected molecular weight is excised and purified. The PCR product is verified to be the selected sequence by subcloning and sequencing the DNA product.

Finally, overlapping oligos of the DNA sequences of SEQ ID NOS:1-155 can be chemically synthesized and used to generate a nucleotide sequence of desired length using PCR methods known in the art.

6(a). Expression and Purification Borrelia polypeptides in E. coli

The bacterial expression vector pQE60 is used for bacterial expression of some of the polypeptide fragements of the present invention. (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311). pQE60 encodes ampicillin antibiotic resistance ("Ampr") and contains a bacterial origin of replication ("ori"), an IPTG inducible promoter, a ribosome binding site ("RBS"), six codons encoding histidine residues that allow affinity purification using nickel-nitrilo-tri-acetic acid ("Ni-NTA") affinity resin (QIAGEN, Inc., *supra*) and suitable single restriction enzyme cleavage sites. These elements are arranged such that an inserted DNA fragment encoding a polypeptide expresses that polypeptide with the six His residues (i.e., a "6

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X His tag") covalently linked to the carboxyl terminus of that polypeptide.

The DNA sequence encoding the desired portion of a *B. burgdorferi* protein of the present invention is amplified from *B. burgdorferi* genomic DNA using PCR oligonucleotide primers which anneal to the 5' and 3' sequences coding for the portions of the *B. burgdorferi* polynucleotide shown in SEQ ID NOS:1-155. Additional nucleotides containing restriction sites to facilitate cloning in the pQE60 vector are added to the 5' and 3' sequences, respectively.

For cloning the mature protein, the 5' primer has a sequence containing an appropriate restriction site followed by nucleotides of the amino terminal coding sequence of the desired *B. burgdorferi* polynucleotide sequence in SEQ ID NOS:1-155. One of ordinary skill in the art would appreciate that the point in the protein coding sequence where the 5' and 3' primers begin may be varied to amplify a DNA segment encoding any desired portion of the complete protein shorter or longer than the mature form. The 3' primer has a sequence containing an appropriate restriction site followed by nucleotides complementary to the 3' end of the polypeptide coding sequence of SEQ ID NOS:1-155, excluding a stop codon, with the coding sequence aligned with the restriction site so as to maintain its reading frame with that of the six His codons in the pQE60 vector.

The amplified *B. burgdorferi* DNA fragment and the vector pQE60 are digested with restriction enzymes which recognize the sites in the primers and the digested DNAs are then ligated together. The *B. burgdorferi* DNA is inserted into the restricted pQE60 vector in a manner which places the *B. burgdorferi* protein coding region downstream from the IPTG-inducible promoter and in-frame with an initiating AUG and the six histidine codons.

The ligation mixture is transformed into competent *E. coli* cells using standard procedures such as those described by Sambrook et al., *supra*.. *E. coli* strain M15/rep4, containing multiple copies of the plasmid pREP4, which expresses the lac repressor and confers kanamycin resistance ("Kanr"), is used in carrying out the illustrative example described herein. This strain, which is only one of many that are suitable for expressing a *B. burgdorferi* polypeptide, is available commercially (QIAGEN, Inc., *supra*). Transformants are identified by their ability to grow on LB agar plates in the presence of ampicillin and kanamycin. Plasmid DNA is isolated from resistant colonies and the identity of the cloned DNA confirmed by restriction analysis, PCR and DNA sequencing.

Clones containing the desired constructs are grown overnight ("O/N") in liquid culture in LB media supplemented with both ampicillin ($100 \,\mu g/ml$) and kanamycin ($25 \,\mu g/ml$). The O/N culture is used to inoculate a large culture, at a dilution of approximately 1:25 to 1:250. The cells are grown to an optical density at 600 nm ("OD600") of between 0.4 and 0.6. Isopropyl- β -D-thiogalactopyranoside ("IPTG") is then added to a final concentration of 1 mM to induce transcription from the lac repressor sensitive promoter, by inactivating the lacI repressor. Cells subsequently are incubated further for 3 to 4 hours. Cells then are harvested by centrifugation.

The cells are then stirred for 3-4 hours at 4°C in 6M guanidine-HCl, pH 8. The cell

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debris is removed by centrifugation, and the supernatant containing the *B. burgdorferi* polypeptide is loaded onto a nickel-nitrilo-tri-acetic acid ("Ni-NTA") affinity resin column (QIAGEN, Inc., *supra*). Proteins with a 6 x His tag bind to the Ni-NTA resin with high affinity are purified in a simple one-step procedure (for details see: The QIAexpressionist, 1995, QIAGEN, Inc., *supra*). Briefly the supernatant is loaded onto the column in 6 M guanidine-HCl, pH 8, the column is first washed with 10 volumes of 6 M guanidine-HCl, pH 8, then washed with 10 volumes of 6 M guanidine-HCl pH 6, and finally the *B. burgdorferi* polypeptide is eluted with 6 M guanidine-HCl, pH 5.

The purified protein is then renatured by dialyzing it against phosphate-buffered saline (PBS) or 50 mM Na-acetate, pH 6 buffer plus 200 mM NaCl. Alternatively, the protein could be successfully refolded while immobilized on the Ni-NTA column. The recommended conditions are as follows: renature using a linear 6M-1M urea gradient in 500 mM NaCl, 20% glycerol, 20 mM Tris/HCl pH 7.4, containing protease inhibitors. The renaturation should be performed over a period of 1.5 hours or more. After renaturation the proteins can be eluted by the addition of 250 mM immidazole. Immidazole is removed by a final dialyzing step against PBS or 50 mM sodium acetate pH 6 buffer plus 200 mM NaCl. The purified protein is stored at 4°C or frozen at -80°C.

The polypeptide of the present invention are also prepared using a non-denaturing protein purification method. For these polypeptides, the cell pellet from each liter of culture is resuspended in 25 mls of Lysis Buffer A at 4°C (Lysis Buffer A = 50 mM Na-phosphate, 300 mM NaCl, 10 mM 2-mercaptoethanol, 10% Glycerol, pH 7.5 with 1 tablet of Complete EDTA-free protease inhibitor cocktail (Boehringer Mannheim #1873580) per 50 ml of buffer). Absorbance at 550 nm is approximately 10-20 O.D./ml. The suspension is then put through three freeze/thaw cycles from -70°C (using a ethanol-dry ice bath) up to room temperature. The cells are lysed via sonication in short 10 sec bursts over 3 minutes at approximately 80W while kept on ice. The sonicated sample is then centrifuged at 15,000 RPM for 30 minutes at 4°C. The supernatant is passed through a column containing 1.0 ml of CL-4B resin to pre-clear the sample of any proteins that may bind to agarose non-specifically, and the flow-through fraction is collected.

The pre-cleared flow-through is applied to a nickel-nitrilo-tri-acetic acid ("Ni-NTA") affinity resin column (Quiagen, Inc., *supra*). Proteins with a 6 X His tag bind to the Ni-NTA resin with high affinity and can be purified in a simple one-step procedure. Briefly, the supernatant is loaded onto the column in Lysis Buffer A at 4°C, the column is first washed with 10 volumes of Lysis Buffer A until the A280 of the eluate returns to the baseline. Then, the column is washed with 5 volumes of 40 mM Imidazole (92% Lysis Buffer A / 8% Buffer B) (Buffer B = 50 mM Na-Phosphate, 300 mM NaCl, 10% Glycerol, 10 mM 2-mercaptoethanol, 500 mM Imidazole, pH of the final buffer should be 7.5). The protein is eluted off of the column with a series of increasing Imidazole solutions made by adjusting the ratios of Lysis Buffer A to Buffer B. Three different concentrations are used: 3 volumes of 75 mM Imidazole, 3 volumes of

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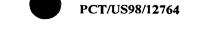
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150 mM Imidazole, 5 volumes of 500 mM Imidazole. The fractions containing the purified protein are analyzed using 8 %, 10 % or 14% SDS-PAGE depending on the protein size. The purified protein is then dialyzed 2X against phosphate-buffered saline (PBS) in order to place it into an easily workable buffer. The purified protein is stored at 4°C or frozen at -80°.

The following alternative method may be used to purify B. burgdorferi expressed in E coli when it is present in the form of inclusion bodies. Unless otherwise specified, all of the following steps are conducted at $4-10^{\circ}$ C.

Upon completion of the production phase of the *E. coli* fermentation, the cell culture is cooled to 4-10°C and the cells are harvested by continuous centrifugation at 15,000 rpm (Heraeus Sepatech). On the basis of the expected yield of protein per unit weight of cell paste and the amount of purified protein required, an appropriate amount of cell paste, by weight, is suspended in a buffer solution containing 100 mM Tris, 50 mM EDTA, pH 7.4. The cells are dispersed to a homogeneous suspension using a high shear mixer.

The cells are then lysed by passing the solution through a microfluidizer (Microfuidics, Corp. or APV Gaulin, Inc.) twice at 4000-6000 psi. The homogenate is then mixed with NaCl solution to a final concentration of 0.5 M NaCl, followed by centrifugation at 7000 x g for 15 min. The resultant pellet is washed again using 0.5M NaCl, 100 mM Tris, 50 mM EDTA, pH 7.4.

The resulting washed inclusion bodies are solubilized with 1.5 M guanidine hydrochloride (GuHCl) for 2-4 hours. After 7000 x g centrifugation for 15 min., the pellet is discarded and the B. burgdorferi polypeptide-containing supernatant is incubated at 4°C overnight to allow further GuHCl extraction.

Following high speed centrifugation (30,000 x g) to remove insoluble particles, the GuHCl solubilized protein is refolded by quickly mixing the GuHCl extract with 20 volumes of buffer containing 50 mM sodium, pH 4.5, 150 mM NaCl, 2 mM EDTA by vigorous stirring. The refolded diluted protein solution is kept at 4°C without mixing for 12 hours prior to further purification steps.

To clarify the refolded *B. burgdorferi* polypeptide solution, a previously prepared tangential filtration unit equipped with 0.16 µm membrane filter with appropriate surface area (e.g., Filtron), equilibrated with 40 mM sodium acetate, pH 6.0 is employed. The filtered sample is loaded onto a cation exchange resin (e.g., Poros HS-50, Perseptive Biosystems). The column is washed with 40 mM sodium acetate, pH 6.0 and eluted with 250 mM, 500 mM, 1000 mM, and 1500 mM NaCl in the same buffer, in a stepwise manner. The absorbance at 280 mm of the effluent is continuously monitored. Fractions are collected and further analyzed by SDS-PAGE.

Fractions containing the B. burgdorferi polypeptide are then pooled and mixed with 4

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volumes of water. The diluted sample is then loaded onto a previously prepared set of tandem columns of strong anion (Poros HQ-50, Perseptive Biosystems) and weak anion (Poros CM-20, Perseptive Biosystems) exchange resins. The columns are equilibrated with 40 mM sodium acetate, pH 6.0. Both columns are washed with 40 mM sodium acetate, pH 6.0, 200 mM NaCl. The CM-20 column is then eluted using a 10 column volume linear gradient ranging from 0.2 M NaCl, 50 mM sodium acetate, pH 6.0 to 1.0 M NaCl, 50 mM sodium acetate, pH 6.5. Fractions are collected under constant A₂₈₀ monitoring of the effluent. Fractions containing the *B. burgdorferi* polypeptide (determined, for instance, by 16% SDS-PAGE) are then pooled.

The resultant *B. burgdorferi* polypeptide exhibits greater than 95% purity after the above refolding and purification steps. No major contaminant bands are observed from Commassie blue stained 16% SDS-PAGE gel when 5 µg of purified protein is loaded. The purified protein is also tested for endotoxin/LPS contamination, and typically the LPS content is less than 0.1 ng/ml according to LAL assays.

6(b). Alternative Expression and Purification Borrelia polypeptides in E. coli

The vector pQE10 is alternatively used to clone and express some of the polypeptides of the present invention for use in the soft tissue and systemic infection models discussed below. The difference being such that an inserted DNA fragment encoding a polypeptide expresses that polypeptide with the six His residues (i.e., a "6 X His tag") covalently linked to the amino terminus of that polypeptide. The bacterial expression vector pQE10 (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311) was used in this example. The components of the pQE10 plasmid are arranged such that the inserted DNA sequence encoding a polypeptide of the present invention expresses the polypeptide with the six His residues (i.e., a "6 X His tag")) covalently linked to the amino terminus.

The DNA sequences encoding the desired portions of a polypeptide of SEQ ID NOS:1-155 were amplified using PCR oligonucleotide primers from genomic *B. burgdorferi* DNA. The PCR primers anneal to the nucleotide sequences encoding the desired amino acid sequence of a polypeptide of the present invention. Additional nucleotides containing restriction sites to facilitate cloning in the pQE10 vector were added to the 5' and 3' primer sequences, respectively.

For cloning a polypeptide of the present invention, the 5' and 3' primers were selected to amplify their respective nucleotide coding sequences. One of ordinary skill in the art would appreciate that the point in the protein coding sequence where the 5' and 3' primers begins may be varied to amplify a DNA segment encoding any desired portion of a polypeptide of the present invention. The 5' primer was designed so the coding sequence of the 6 X His tag is aligned with the restriction site so as to maintain its reading frame with that of *B. burgdorferi* polypeptide. The 3' was designed to include an stop codon. The amplified DNA fragment was then cloned, and the protein expressed, as described above for the pQE60 plasmid.

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The DNA sequences of SEQ ID NOS:1-155 encoding amino acid sequences may also be cloned and expressed as fusion proteins by a protocol similar to that described directly above, wherein the pET-32b(+) vector (Novagen, 601 Science Drive, Madison, WI 53711) is preferentially used in place of pQE10.

The above methods are not limited to the polypeptide fragements actually produced. The above method, like the methods below, can be used to produce either full length polypeptides or desired fragements therof.

6(c). Alternative Expression and Purification of Borrelia polypeptides in E. coli

The bacterial expression vector pQE60 is used for bacterial expression in this example (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311). However, in this example, the polypeptide coding sequence is inserted such that translation of the six His codons is prevented and, therefore, the polypeptide is produced with no 6 X His tag.

The DNA sequence encoding the desired portion of the *B. burgdorferi* amino acid sequence is amplified from an *B. burgdorferi* genomic DNA prep the deposited DNA clones using PCR oligonucleotide primers which anneal to the 5' and 3' nucleotide sequences corresponding to the desired portion of the *B. burgdorferi* polypeptides. Additional nucleotides containing restriction sites to facilitate cloning in the pQE60 vector are added to the 5' and 3' primer sequences.

For cloning a *B. burgdorferi* polypeptides of the present invention, 5' and 3' primers are selected to amplify their respective nucleotide coding sequences. One of ordinary skill in the art would appreciate that the point in the protein coding sequence where the 5' and 3' primers begin may be varied to amplify a DNA segment encoding any desired portion of a polypeptide of the present invention. The 3' and 5' primers contain appropriate restriction sites followed by nucleotides complementary to the 5' and 3' ends of the coding sequence respectively. The 3' primer is additionally designed to include an in-frame stop codon.

The amplified *B. burgdorferi* DNA fragments and the vector pQE60 are digested with restriction enzymes recognizing the sites in the primers and the digested DNAs are then ligated together. Insertion of the *B. burgdorferi* DNA into the restricted pQE60 vector places the *B. burgdorferi* protein coding region including its associated stop codon downstream from the IPTG-inducible promoter and in-frame with an initiating AUG. The associated stop codon prevents translation of the six histidine codons downstream of the insertion point.

The ligation mixture is transformed into competent *E. coli* cells using standard procedures such as those described by Sambrook et al. *E. coli* strain M15/rep4, containing multiple copies of the plasmid pREP4, which expresses the lac repressor and confers kanamycin resistance ("Kanr"), is used in carrying out the illustrative example described herein. This strain, which is only one of many that are suitable for expressing *B. burgdorferi* polypeptide, is available commercially (QIAGEN, Inc., *supra*). Transformants are identified by their ability to grow on

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LB plates in the presence of ampicillin and kanamycin. Plasmid DNA is isolated from resistant colonies and the identity of the cloned DNA confirmed by restriction analysis, PCR and DNA sequencing.

Clones containing the desired constructs are grown overnight ("O/N") in liquid culture in LB media supplemented with both ampicillin (100 μ g/ml) and kanamycin (25 μ g/ml). The O/N culture is used to inoculate a large culture, at a dilution of approximately 1:25 to 1:250. The cells are grown to an optical density at 600 nm ("OD600") of between 0.4 and 0.6. isopropyl-b-D-thiogalactopyranoside ("IPTG") is then added to a final concentration of 1 mM to induce transcription from the *lac* repressor sensitive promoter, by inactivating the lacI repressor. Cells subsequently are incubated further for 3 to 4 hours. Cells then are harvested by centrifugation.

To purify the *B. burgdorferi* polypeptide, the cells are then stirred for 3-4 hours at 4°C in 6M guanidine-HCl, pH 8. The cell debris is removed by centrifugation, and the supernatant containing the *B. burgdorferi* polypeptide is dialyzed against 50 mM Na-acetate buffer pH 6, supplemented with 200 mM NaCl. Alternatively, the protein can be successfully refolded by dialyzing it against 500 mM NaCl, 20% glycerol, 25 mM Tris/HCl pH 7.4, containing protease inhibitors. After renaturation the protein can be purified by ion exchange, hydrophobic interaction and size exclusion chromatography. Alternatively, an affinity chromatography step such as an antibody column can be used to obtain pure *B. burgdorferi* polypeptide. The purified protein is stored at 4°C or frozen at -80°C.

The following alternative method may be used to purify *B. burgdorferi* polypeptides expressed in *E coli* when it is present in the form of inclusion bodies. Unless otherwise specified, all of the following steps are conducted at 4-10°C.

Upon completion of the production phase of the *E. coli* fermentation, the cell culture is cooled to 4-10°C and the cells are harvested by continuous centrifugation at 15,000 rpm (Heraeus Sepatech). On the basis of the expected yield of protein per unit weight of cell paste and the amount of purified protein required, an appropriate amount of cell paste, by weight, is suspended in a buffer solution containing 100 mM Tris, 50 mM EDTA, pH 7.4. The cells are dispersed to a homogeneous suspension using a high shear mixer.

The cells ware then lysed by passing the solution through a microfluidizer (Microfuidics, Corp. or APV Gaulin, Inc.) twice at 4000-6000 psi. The homogenate is then mixed with NaCl solution to a final concentration of 0.5 M NaCl, followed by centrifugation at 7000 x g for 15 min. The resultant pellet is washed again using 0.5M NaCl, 100 mM Tris, 50 mM EDTA, pH 7.4.

The resulting washed inclusion bodies are solubilized with 1.5 M guanidine hydrochloride (GuHCl) for 2-4 hours. After 7000 x g centrifugation for 15 min., the pellet is discarded and the B. burgdorferi polypeptide-containing supernatant is incubated at 4°C overnight to allow further GuHCl extraction.

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Following high speed centrifugation (30,000 x g) to remove insoluble particles, the GuHCl solubilized protein is refolded by quickly mixing the GuHCl extract with 20 volumes of buffer containing 50 mM sodium, pH 4.5, 150 mM NaCl, 2 mM EDTA by vigorous stirring. The refolded diluted protein solution is kept at 4°C without mixing for 12 hours prior to further purification steps.

To clarify the refolded *B. burgdorferi* polypeptide solution, a previously prepared tangential filtration unit equipped with 0.16 µm membrane filter with appropriate surface area (e.g., Filtron), equilibrated with 40 mM sodium acetate, pH 6.0 is employed. The filtered sample is loaded onto a cation exchange resin (e.g., Poros HS-50, Perseptive Biosystems). The column is washed with 40 mM sodium acetate, pH 6.0 and eluted with 250 mM, 500 mM, 1000 mM, and 1500 mM NaCl in the same buffer, in a stepwise manner. The absorbance at 280 mm of the effluent is continuously monitored. Fractions are collected and further analyzed by SDS-PAGE.

Fractions containing the *B. burgdorferi* polypeptide are then pooled and mixed with 4 volumes of water. The diluted sample is then loaded onto a previously prepared set of tandem columns of strong anion (Poros HQ-50, Perseptive Biosystems) and weak anion (Poros CM-20, Perseptive Biosystems) exchange resins. The columns are equilibrated with 40 mM sodium acetate, pH 6.0. Both columns are washed with 40 mM sodium acetate, pH 6.0, 200 mM NaCl. The CM-20 column is then eluted using a 10 column volume linear gradient ranging from 0.2 M NaCl, 50 mM sodium acetate, pH 6.0 to 1.0 M NaCl, 50 mM sodium acetate, pH 6.5. Fractions are collected under constant A₂₈₀ monitoring of the effluent. Fractions containing the *B. burgdorferi* polypeptide (determined, for instance, by 16% SDS-PAGE) are then pooled.

The resultant *B. burgdorferi* polypeptide exhibits greater than 95% purity after the above refolding and purification steps. No major contaminant bands are observed from Commassie blue stained 16% SDS-PAGE gel when 5 µg of purified protein is loaded. The purified protein is also tested for endotoxin/LPS contamination, and typically the LPS content is less than 0.1 ng/ml according to LAL assays.

6(d). Cloning and Expression of B. burgdorferi in Other Bacteria

B. burgdorferi polypeptides can also be produced in: B. burgdorferi using the methods of S. Skinner et al., (1988) Mol. Microbiol. 2:289-297 or J. I. Moreno (1996) Protein Expr. Purif. 8(3):332-340; Lactobacillus using the methods of C. Rush et al., 1997 Appl. Microbiol. Biotechnol. 47(5):537-542; or in Bacillus subtilis using the methods Chang et al., U.S. Patent No. 4,952,508.

7. Cloning and Expression in COS Cells

A B. burgdorferi expression plasmid is made by cloning a portion of the DNA encoding a

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B. burgdorferi polypeptide into the expression vector pDNAI/Amp or pDNAIII (which can be obtained from Invitrogen, Inc.). The expression vector pDNAI/amp contains: (1) an E. coli origin of replication effective for propagation in E. coli and other prokaryotic cells; (2) an ampicillin resistance gene for selection of plasmid-containing prokaryotic cells; (3) an SV40 origin of replication for propagation in eukaryotic cells; (4) a CMV promoter, a polylinker, an SV40 intron; (5) several codons encoding a hemagglutinin fragment (i.e., an "HA" tag to facilitate purification) followed by a termination codon and polyadenylation signal arranged so that a DNA can be conveniently placed under expression control of the CMV promoter and operably linked to the SV40 intron and the polyadenylation signal by means of restriction sites in the polylinker. The HA tag corresponds to an epitope derived from the influenza hemagglutinin protein described by Wilson et al. 1984 Cell 37:767. The fusion of the HA tag to the target protein allows easy detection and recovery of the recombinant protein with an antibody that recognizes the HA epitope. pDNAIII contains, in addition, the selectable neomycin marker.

A DNA fragment encoding a *B. burgdorferi* polypeptide is cloned into the polylinker region of the vector so that recombinant protein expression is directed by the CMV promoter. The plasmid construction strategy is as follows. The DNA from a *B. burgdorferi* genomic DNA prep is amplified using primers that contain convenient restriction sites, much as described above for construction of vectors for expression of *B. burgdorferi* in *E. coli*. The 5' primer contains a Kozak sequence, an AUG start codon, and nucleotides of the 5' coding region of the *B. burgdorferi* polypeptide. The 3' primer, contains nucleotides complementary to the 3' coding sequence of the *B. burgdorferi* DNA, a stop codon, and a convenient restriction site.

The PCR amplified DNA fragment and the vector, pDNAI/Amp, are digested with appropriate restriction enzymes and then ligated. The ligation mixture is transformed into an appropriate $E.\ coli$ strain such as SURETM (Stratagene Cloning Systems, La Jolla, CA 92037), and the transformed culture is plated on ampicillin media plates which then are incubated to allow growth of ampicillin resistant colonies. Plasmid DNA is isolated from resistant colonies and examined by restriction analysis or other means for the presence of the fragment encoding the $B.\ burgdorferi$ polypeptide

For expression of a recombinant *B. burgdorferi* polypeptide, COS cells are transfected with an expression vector, as described above, using DEAE-dextran, as described, for instance, by Sambrook et al. (*supra*). Cells are incubated under conditions for expression of *B. burgdorferi* by the vector.

Expression of the *B. burgdorferi*-HA fusion protein is detected by radiolabeling and immunoprecipitation, using methods described in, for example Harlow et al., *supra*.. To this end, two days after transfection, the cells are labeled by incubation in media containing ³⁵S-cysteine for 8 hours. The cells and the media are collected, and the cells are washed and the lysed with detergent-containing RIPA buffer: 150 mM NaCl, 1% NP-40, 0.1% SDS, 1% NP-40, 0.5% DOC, 50 mM TRIS, pH 7.5, as described by Wilson et al. (*supra*). Proteins are

precipitated from the cell lysate and from the culture media using an HA-specific monoclonal antibody. The precipitated proteins then are analyzed by SDS-PAGE and autoradiography. An expression product of the expected size is seen in the cell lysate, which is not seen in negative controls.

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8. Cloning and Expression in CHO Cells

The vector pC4 is used for the expression of *B. burgdorferi* polypeptide in this example. Plasmid pC4 is a derivative of the plasmid pSV2-dhfr (ATCC Accession No. 37146). The plasmid contains the mouse DHFR gene under control of the SV40 early promoter. Chinese hamster ovary cells or other cells lacking dihydrofolate activity that are transfected with these plasmids can be selected by growing the cells in a selective medium (alpha minus MEM, Life Technologies) supplemented with the chemotherapeutic agent methotrexate. The amplification of the DHFR genes in cells resistant to methotrexate (MTX) has been well documented. *See, e.g.*, Alt et al., 1978, J. Biol. Chem. 253:1357-1370; Hamlin et al., 1990, Biochem. et Biophys. Acta, 1097:107-143; Page et al., 1991, Biotechnology 9:64-68. Cells grown in increasing concentrations of MTX develop resistance to the drug by overproducing the target enzyme, DHFR, as a result of amplification of the DHFR gene. If a second gene is linked to the DHFR gene, it is usually co-amplified and over-expressed. It is known in the art that this approach may be used to develop cell lines carrying more than 1,000 copies of the amplified gene(s). Subsequently, when the methotrexate is withdrawn, cell lines are obtained which contain the amplified gene integrated into one or more chromosome(s) of the host cell.

Plasmid pC4 contains the strong promoter of the long terminal repeat (LTR) of the Rouse Sarcoma Virus, for expressing a polypeptide of interest, Cullen, et al. (1985) Mol. Cell. Biol. 5:438-447; plus a fragment isolated from the enhancer of the immediate early gene of human cytomegalovirus (CMV), Boshart, et al., 1985, Cell 41:521-530. Downstream of the promoter are the following single restriction enzyme cleavage sites that allow the integration of the genes: Bam HI, Xba I, and Asp 718. Behind these cloning sites the plasmid contains the 3' intron and polyadenylation site of the rat preproinsulin gene. Other high efficiency promoters can also be used for the expression, e.g., the human \(\mathcal{B} \)-actin promoter, the SV40 early or late promoters or the long terminal repeats from other retroviruses, e.g., HIV and HTLVI. Clontech's Tet-Off and Tet-On gene expression systems and similar systems can be used to express the B. burgdorferi polypeptide in a regulated way in mammalian cells (Gossen et al., 1992, Proc. Natl. Acad. Sci. USA 89:5547-5551. For the polyadenylation of the mRNA other signals, e.g., from the human growth hormone or globin genes can be used as well. Stable cell lines carrying a gene of interest integrated into the chromosomes can also be selected upon co-transfection with a selectable marker such as gpt, G418 or hygromycin. It is advantageous to use more than one selectable marker in the beginning, e.g., G418 plus methotrexate.

The plasmid pC4 is digested with the restriction enzymes and then dephosphorylated using calf intestinal phosphates by procedures known in the art. The vector is then isolated from

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a 1% agarose gel. The DNA sequence encoding the *B. burgdorferi* polypeptide is amplified using PCR oligonucleotide primers corresponding to the 5' and 3' sequences of the desired portion of the gene. A 5' primer containing a restriction site, a Kozak sequence, an AUG start codon, and nucleotides of the 5' coding region of the *B. burgdorferi* polypeptide is synthesized and used. A 3' primer, containing a restriction site, stop codon, and nucleotides complementary to the 3' coding sequence of the *B. burgdorferi* polypeptides is synthesized and used. The amplified fragment is digested with the restriction endonucleases and then purified again on a 1% agarose gel. The isolated fragment and the dephosphorylated vector are then ligated with T4 DNA ligase. *E. coli* HB101 or XL-1 Blue cells are then transformed and bacteria are identified that contain the fragment inserted into plasmid pC4 using, for instance, restriction enzyme analysis.

Chinese hamster ovary cells lacking an active DHFR gene are used for transfection. Five μg of the expression plasmid pC4 is cotransfected with 0.5 μg of the plasmid pSVneo using a lipid-mediated transfection agent such as Lipofectin™ or LipofectAMINE.™ (LifeTechnologies Gaithersburg, MD). The plasmid pSV2-neo contains a dominant selectable marker, the neo gene 15 from Tn5 encoding an enzyme that confers resistance to a group of antibiotics including G418. The cells are seeded in alpha minus MEM supplemented with 1 mg/ml G418. After 2 days, the cells are trypsinized and seeded in hybridoma cloning plates (Greiner, Germany) in alpha minus MEM supplemented with 10, 25, or 50 ng/ml of methotrexate plus 1 mg/ml G418. After about 10-14 days single clones are trypsinized and then seeded in 6-well petri dishes or 10 ml flasks 20 using different concentrations of methotrexate (50 nM, 100 nM, 200 nM, 400 nM, 800 nM). Clones growing at the highest concentrations of methotrexate are then transferred to new 6-well plates containing even higher concentrations of methotrexate (1 µM, 2 µM, 5 µM, 10 mM, 20 mM). The same procedure is repeated until clones are obtained which grow at a concentration of 25 100-200 µM. Expression of the desired gene product is analyzed, for instance, by SDS-PAGE and Western blot or by reversed phase HPLC analysis.

The disclosure of all publications (including patents, patent applications, journal articles, laboratory manuals, books, or other documents) cited herein are hereby incorporated by reference in their entireties.

The present invention is not to be limited in scope by the specific embodiments described herein, which are intended as single illustrations of individual aspects of the invention. Functionally equivalent methods and components are within the scope of the invention, in addition to those shown and described herein and will become apparant to those skilled in the art from the foregoing description and accompanying drawings. Such modifications are intended to fall within the scope of the appended claims.

Borrelia burgdorferi - Putative coding regions of novel proteins similar to know proteins

TABLE 1.

Contig ORF	ORF	Start (nt)	Stop	match	match gene name	% sim	%
<u>e</u>	<u> </u>		(nt)	ac			ident
I	6	100363	100184	gil500722	similar to entire extracellular domain of glycine receptors	100	99
					[Caenorhabditis elegans]		
	537		513608 gil4	→ 1	[ribosomal protein S12 [Streptococcus pneumoniae]	92	85
	283		270849 gil	gil1001376	ATP-dependent protease ATPase subunit [Synechocystis sp.]	89	75
1	847	7		gil467373	ribosomal protein S18 [Bacillus subtilis]	98	
	28			gil1573896	ribosomal protein L27 (rpL27) [Haemophilus influenzae]	85	
Ī	732	687538	[][86753]	gil1591672	phosphate transport system ATP-binding protein [Methanococcus	84	99
I	788	739513	739232	gil142459	initiation factor 1 [Bacillus subtilis]	84	89
I	096	901448	901780 gnIII	gnllPIDle2437	PIDle2437 ORF YGL149w [Saccharomyces cerevisiae]	84	
			- 1	69			
	760	717009		715843 gil623028	orf 361; ranslated orf similarity to SW: RFI_SALTY peptide chain release factor 1 of Salmonella typhimurium [Coxiella burnetii]	83	09
1	115		115312	115312 gil695315	NADH dehydrogenase subunit [Digitalis grandiflora]	82	58
	184	178954	176918 bbs	pps157690	EF-G=elongation factor G [Thermotoga maritima, Peptide, 682	82	63
_					aaj [i nermotoga maritima]		
	447	`	425453	딦	Ndk [Bacillus subtilis]	82	26
	201	194702	194103 gil5	gil530438	arabinose transport protein [Mycoplasma capricolum]	81	53
	477	446671	445589 gil8	gil8	fructose 1,6-bisphosphate aldolase [Escherichia coli]	81	61
	601	569453	568650	gil3	transmembrane protein [Escherichia coli]	81	56
	887		837224 gil1	gil1237019	Srb [Bacillus subtilis]	81	52
	886		839497	Ei]	peptide chain release factor 2 [Salmonella typhimurium]	81	65
	968	∞	845440	gi!]	aminopeptidase [Bacillus subtilis]	81	09
	9		68890 gil 1		DNA mismatch repair protein [Thermotoga maritima]	08	59
	354		349157 gill		chemotaxis protein CheY [Treponema pallidum]	08	42
	423	409238	408855	gnllPIDle2118 29	PIDIe2118 50S ribosomal protein L14 [Odontella sinensis]	08	19
1	426	410130	409711	gil1652420	50S ribosomal protein L16 [Synechocystis sp.]	08	59
	507		482936	gil515924	glucosyltransferase [Saccharomyces cerevisiae]	08	40
	534	505081	505467	pirlA027711R	ribosomal protein L7/L12 - Micrococcus luteus	80	19

		DOLLOHA DUI BUOLICH - L'U	DOILGIA DU GUOTELL - FUIGHTVE COUING TEGIOUS OF HOVEINS SIMILAR TO KNOW PROTEINS		
597	567506	566532 gil5	OppF gene product [Bacillus subtilis]	80	59
9	11241	9994 gnliPIDle2426 14	PIDIe2426 arginine deiminase [Clostridium perfringens]	6/	62
478	447926	446835 gnIIPIDIe2881 24	glucose epimerase [Bacillus thuringiensis]	79	99
804	758549	757704	glucosamine-6-phosphate deaminase protein [Escherichia coli]	79	09
25	31595	31894	similar to dihydropryridine-sensitive I-type, skeletal muscle calcium channel alpha-1 subunit (SP:CIC1_RABIT, P07293) [Caenorhabditis elegans]	78	57
134	134667	134323 gill:	cecropin D [Hyalophora cecropia]	78	50
230	215177	216028 gnlll 37	OIDle 2655 Dna J-homologue [Thermus aquaticus thermophilus]	78	59
531	503406	Į.	ribosomal protein L11 [Thermus aquaticus thermophilus]	78	58
867	817849	819579 gil9	Na+ -ATPase alpha subunit [Enterococcus hirae]	782	9
127	127383	127745 gil5	heat shock protein 60 (GroEL) like protein [Porphyromonas gingivalis]	77	09
190	182991	182251 gil 1235682	mevalonate pyrophosphate decarboxylase [Homo sapiens]	77	51
225	213158	212388 gil1651340	Phosphoglycerate mutase 1 [Escherichia coli]	11	59
284	272770	272165 gill(ATP-dependent protease ClpP [Synechocystis sp.]	77	62
324	318280	314789 gill 5	DNA polymerase III, alpha chain (dnaE) [Haemophilus influenzae]	11	58
555	530150		transfer RNA-Tyr synthetase [Bacillus subtilis]	77	52
770	722470	722892 gil16	hypothetical protein [Synechocystis sp.]	77	54
833	790115	790909 gnllP 86	[Dle2488 unknown [Mycobacterium tuberculosis]	11	56
52	62205	61918 gnllPIDle1189 66	61918 gnllPIDle1189 ribosomal protein S15 [Thermus aquaticus thermophilus]	76	09
144	141975	1	KHS toxin, killer heat sensitive toxin=KHS [Saccharomyces cerevisiae, Peptide, 708 aa] [Saccharomyces cerevisiae]	76	38
293	280702		VP2 protein [Bluetongue virus 9]	76	47
323	314795	314199 gil1651915	hypothetical protein [Synechocystis sp.]	76	48
362	356749	355508 011633147	ribose-phosphate nyrophosphokinase (Racillus caldolyticus)	76	VV

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57	58	49	50	56	49	43	53	51	41	52	53	55	53	47	54		99	63	50	53	54	51	49	51	51	41	42
74	74	74	74	73	73	73	73	73	73	73	73	73	73	73	73		73	73	73	72	72	72	72	72	72	72	77
Putative coding regions of novel proteins similar to know proteins S-adenosylmethionine synthetase [Staphylococcus aureus]	enolase [Bacillus subtilis]	hypothetical protein [Synechocystis sp.]	UDP-glucose pyrophosphorylase [Bacillus subtilis]	excinuclease ABC subunit A [Synechocystis sp.]	sensor kinase [Bacillus subtilis]	Erg8p [Saccharomyces cerevisiae]	'ORF' [Escherichia coli]	ORF YLR069c [Saccharomyces cerevisiae]	hypothetical [Haemonhillis influenzae]	hemolysin (Serpulina hyodysenteriae)	glycoprotein 120 [Simian immunodeficiency virus]	sporulation protein [Bacillus subtilis]	60 kda antigen [Borrelia coriaceae, C053, ATCC 4338, Peptide, 514 aal [Borrelia coriaceae]	type-I signal peptidase SpsB [Staphylococcus aureus]	unknown [Mycobacterium tuberculosis]		Similar to Seryl-tRNA synthetase [Saccharomyces cerevisiae]	le2436 ORF YGR248w [Saccharomyces cerevisiae]	hypothetical protein [Synechocystis sp.]	hemolysin [Serpulina hyodysenteriae]	NtrC/NifA-like protein regulator [Escherichia coli]	Similar to Saccharomyces cerevisiae SUA5 protein [Bacillus subtilis]	transcription-repair coupling factor [Bacillus subtilis]	ribosomal protein S4 (rpS4) [Haemophilus influenzae]	Ion protease [Bacillus brevis]	haemolysin releasing protein (AA 1-548) [Vibrio cholerae]	CTP synthase [Methanococcus januaschii]
Borrelia burgdorferi - 1	2 5	680489 gil1651	7 701173 gil289287	122/1	104947 gil5143	181102 gil8876	Ì	6 361078 gnllPIDle2457		533672 gil5111	548045 gil4061	L	5 570729 bbs 161785	5 633648 gil1595810	7 651727 gnllPIDIe2684	96	680499 gil5007	682899 gnllPID 81	844964 gil1652	26497 gil5111	106305 gil6199	5 135055 gil556881	26030) 268221 gil1573812		318363 gil 4836	321053 9111 591801
52456	56567	681529	702297	20409	103790	182064	303616	358916	424047	53137.	548257	568379	572375	634175	654267		679186	682189	845455	24242	104935	134036	256925	267529	270922	319544	322678
549	595	720	745	13	86	188	314	998	444	556	918	298	604	674	692	1	719	725	895	16	66	133	270	280	282	325	328
		1	1	1	I	1	1			I	1	1	1	T	1			 	1	1	1		1	-1	-	=	_



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	341182 gil14568	341460
937 M. genitalium predicted coding region MG246 [Mycoplasma genitalium]	<u>6</u>	50
	3($g_{\mathbf{j}}$
33 ribosomal protein L13 (rpL13)		00
sporulation protein (spoIIIE) [Haemophilus influenzae	m	ac
	\sim	0.0
	\sim 1	08
asparaginyl-tRNA synthetase [Synechocystis sp.	\sim	<u>.</u> 29
UvrB [Helicobacter pylori]	32	20407 gil1737482
beta-b protein [Barley stripe mosaic virus]	\simeq	8
ORF9 [Rhizobium meliloti]	~ 1	g
	X)	gi
similar to the	_	496383 gil459009
S5 glycyl-tRNA synthetase - Thermus thermophilus	7	530156 pirlS58522lS5 8522
pyruvate kinase [Bacillus stearothermophilus		50
ORF1 [Synechococcus elongatus		90
secretion protein SecY (AA 1-482) [Mycoplasma capricolum		681561 gil44228
ORF for methionine amino peptidase [Bacillus subtilis]		,
queA [Escherichia coli]	I	<u>22</u>
Cdc28p [Schizosaccharomyces pombe]	$\mathcal{C}_{\mathbf{J}}$	ᇳ
o287 [Escherichia coli	.	G
flgG protein product (AA 1-260) [Salmonella typhimurium		95220 gil47677
H. influenzae predicted coding region H11534 [Haemophilus influenzae]		128569 gil1574387
(AE000012) Mycoplasma pneumoniae, phosphocarrier protein HPr; similar to GenBank Accession Number A49683, from M	<u></u>	441330 gil1673757
_	- 11	
IRL 50S RIBOSOMAL PROTEIN L1 (BL1)	\sim \sim 1	504529 splQ06/9/IRL 1_BACSU

			Borrelia burgdor	feri - Puta	dorferi - Putative coding regions of novel proteins similar to know proteins		
	594	563858	564280 gil6061	06169	30S ribosomal subunit protein S9 [Escherichia coli]	70	56
	622	591070	591606 gil1539	53906	CheW protein [Salmonella typhimurium]	70	48
	703	664161		PIDle2839	glycerol kinase [Sulfolobus solfataricus]	70	09
1	726	682886	682659 gil8368	36815	cdc4 gene product which is essential for initiation of DNA replication in yeast [Saccharomyces cerevisiae]	0/	35
	99/	720854	721417 gil4361	36165	Dsg [Myxococcus xanthus]	70	47
1	768	721649	722008 gnllPIL 81)le2549	PDle2549 ribosomal protein L20 [Bacillus subtilis]	70	48
	965	904395	905465 gill 100	00074	tryptophanyl-tRNA synthetase [Clostridium longisporum]	70	47
1	87	98696	97336 gil1		asparagine-rich protein [Plasmodium falciparum]	69	46
1	110	112658	113602 gil10		ABC transporter [Synechocystis sp.]	69	46
	181	174037	173762 pirl(471)	7154IC	ribosomal protein S16 - Bacillus subtilis	69	52
	233	219872	gill	001493	protein-export membrane protein SecD [Synechocystis sp.]	69	47
1	234	220245	gill		ORF11 [Enterococcus faecalis]	69	32
I	373	366148	gill		hypothetical [Haemophilus influenzae]	69	48
	419	407781			ribosomal S8 protein [Thermus aquaticus thermophilus]	69	46
1	517	489315	gills		fructose enzyme II [Rhodobacter capsulatus]	69	42
1	009	568891	7		sporulation protein [Bacillus subtilis]	69	44
1	733	860689	687536 gil 1303		YqgI [Bacillus subtilis]	69	46
	874	826778	827746 pirlS08 8183	08	L-lactate dehydrogenase (EC 1.1.1.27) X - Bacillus psychrosaccharolyticus	69	20
	894	844392	844547 gil1592324		M. jannaschii predicted coding region MJ1172 [Methanococcus jannaschii]	69	53
1	934	879725	879237 gil 1535		ORF (19K protein) [Enterococcus faecalis]	69	42
-	46	61118	57976 gil8095		unknown [Saccharomyces cerevisiae]	89	36
	107	110374	111513 gnlIPIDIe2559 43)le2559	M04B2.4 [Caenorhabditis elegans]	89	48
1	132	133978	133148 gil1001	001663	rare lipoprotein A [Synechocystis sp.]	89	53
	142	141239	142642 gnIIPID 74)le2338	Mole 2338 hypothetical protein [Bacillus subtilis]	89	45
1	148	145381	144005 gil5585	8574	pyrophosphatefructose-6-phosphate 1-phosphotransferase	89	48

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	į	آمِ	tative coding regions of novel proteins similar to know proteins		
1 358		2	11546788 tar-1 [Trichostrongylus colubriformis]	99	55
1 404		398324 gil296626	[hemolysin [Serpulina hyodysenteriae]	99	53
1 	1 461335	460550 gil45713	P.putida genes rpmH, rnpA, 9k, 60k, 50k, gidA, gidB, uncl and uncB [Pseudomonas putida]	99	41
1 513			methyltransferase (cheR; EC 2.1.1.24) [Salmone]]a typhimirium]	99	42
1 552	2 526495	527316	A 'c' was inserted after nt 369 (=nt 10459 in genomic sequence (M10126)) to correct -1 frameshift probably due to get	99	40
			compression [Leishmania tarentolae]		
1 611		581069 gi	putative pectinesterase [Medicago sativa]	99	33
 1 627	7 595395	596288 gr	ullPIDle2639 OrfD [Streptococcus pneumoniae]	99	47
1 772	2 723788	723522 gil1762342	could accelerate degradation of certain transcripts [Bacillus	99	47
1 816	6 770251	770060 gil393266	SUDTILIS glycerol ester hydrolase [Stanhylococcus aureus]	97	,
1 841	195927	기교	novel hemolytic factor [Bacillus cereus]	000	22
1 882	2 835002	834262 gil862629	similar to the ATP-binding transport protein family [Buchnera	99	404
-			aphidicola]	3	}
1 73		87619 gil39656	spoVG gene product [Bacillus megaterium]	65	40
1 97			phosphatidylserine decarboxylase [Bacillus subtilis]	65	39
100		gi	ClpP [Yersinia enterocolitica]	65	42
1 159		gi	penicillin-binding protein 2 (pbp2) [Haemophilus influenzae]	65	4
1 172		169325 gil1146238	poly(A) polymerase [Bacillus subtilis]	65	38
708		<u> </u>	bacterial cell wall hydrolase [Enterococcus faecalis]	65	43
1 333		346553 gill 574651	DNA ligase (lig) [Haemophilus influenzae]	65	45
1 696		655781 gil1651216	Pz-peptidase [Bacillus licheniformis]	65	47
1 /41		<u>8</u>	DNA mismatch repair protein [Aquifex pyrophilus]	65	45
1 846		20		65	45
1 952		g	gyrase A [Helicobacter pylori]	65	4
1 936		gi]]	leader peptidase I [Synechocystis sp.]	65	04
1 961		50	YbbQ [Bacillus subtilis]	65	48
1 963	5	904407 gil 1573307	hypothetical [Haemophilus influenzae]	65	4
11 : 37	47101	45683 gil556014	UDP-N-acetyl muramate-alanine ligase [Bacillus subtilis]	179	146

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41 43 47 47 47	33 30	52 44 44 45 45 45 45	42 42 41	38 42 42 41 41
4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	2 2 2 3	2 4 4 4 4 4	64 64	63 64 66 66
Putative coding regions of novel proteins similar to know proteins rhoptry protein [Plasmodium yoelii] valyl-tRNA synthetase (valS) [Haemophilus influenzae] threonyl-tRNA synthetase (thrS; EC 6.1.1.3) [Escherichia coli] acyl carrier protein [Synechocystis sp.] lipopolysaccharide core biosynthesis protein (kdtB) [Haemophilus influenzae] tRNA (guanine-N1)-methyltransferase [Mycoplasma genitalium] 88 unknown [Mycobacterium tuberculosis]	ORF2136 [Marchantia polymorpha] N-acetylmuramoyl-L-alanine amidase [Synechocystis sp.] hypothetical protein (GB:U00021_5) [Mycoplasma genitalium] transmembrane protein [Escherichia coli]	unknown [Bacillus subtilis] cheW peptide [Escherichia coli] monophosphatase [Synechocystis sp.] DNA polymerase III subunit [Bacillus subtilis] protein-glutamate methylesterase (EC 3.1.1.61) - Salmonella typhimurium dipeptide transport system permease protein (dppB) [Haemophilus		hypothetical [Haemophilus influenzae] glutamate synthase [Escherichia coli] v-type Na-ATPase [Enterococcus hirae] methionyl-tRNA formyltransferase [Escherichia coli] thioredoxin [Arabidopsis thaliana] SbcC (AA 1-1048) [Escherichia coli]
burgdorferi - gil 1041785 gil 1574225 gil 1574225 gil 1574225 gil 157366 gil 1573650 gil 1046163 gil 1046163 gil 1046163 gil 1046163 gil 1046163	197436 gil11665 205761 gil1652866 229036 gil1046160 230967 gil147336	253723 gild67430 332783 gil145520 375565 gil1653737 426437 gil467409 483998 pirlA00547IX YEBET 569451 gil1574678	gil1001335 gnllPIDle28 60 gnllPIDle25 07	795211 gil1573939 812853 gil396314 823339 gil472918 851615 gil581088 853884 gil992960 31444 gil42914
			64022 71015 77196	795211 812853 823339 851615 853884 31444
72211 131969 152924 170326 171105 173033 173033	197654 206795 228146 230149	253160 333349 376509 428137 484558 570416	637996 709637 771784	793892 811972 821501 850668 853492 34314
130 130 174 175 178 180	207 217 244 246	267 340 384 449 510 603	679 753 817	839 . 861 870 901 904

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		l	63	63	63	63	63	63	63	63	63	63	63	63	63	63	63	63	63	63	62	62	62	62	62
			[luenzae]										visiae]			uency					snl				
gdorferi - Putative coding regions of novel proteins similar to know proteins 1652022 GTP-binding protein [Synechocystis sp.]	ORF2136 [Marchantia polymorpha]	oxygen independent coprophorphyrinogen III oxidase [Synechocystis sp.]	protein-export membrane protein (secF) [Haemophilus influenzae]	SPERMIDINE/PUTRESCINE TRANSPORT SYSTEM PERMEASE PROTEIN POTC.	DJ-1 protein [Homo sapiens]	DD-carboxypeptidase [Bacillus subtilis]	mating type a-1 protein [Neurospora crassa]	TRAB [Plasmid pPD1]	GLUTAMYL-TRNA SYNTHETASE (EC 6.1.1.17) (GLUTAMATETRNA LIGASE) (GLURS).	carboxyl-terminal protease [Synechocystis sp.]	Bts1p [Saccharomyces cerevisiae]	EC 1.1.99.5 [Mus musculus]	glycerol 3 phosphate dehydrogenase [Saccharomyces cerevisiae	glycerol uptake facilitator [Bacillus subtilis]	ORF 4 (AA 1-198); 20 kD [Escherichia coli]	putative integral membrane protease required for high frequency lysogenization by bacteriophage lambda [Escherichia coli]	HflK [Vibrio parahaemolyticus]	stringent response-like protein [Streptococcus equisimilis]	transcription elongation factor [Escherichia coli]	basic membrane protein precursor [Treponema pallidum]	H. influenzae predicted coding region H10594 [Haemophilus influenzae]	pantothenate metabolism flavoprotein (dfp) [Haemophilus influenzae]	ORF2 gene product [Bacillus subtilis]	hypothetical protein [Synechocystis sp.]	PIDle2118 50S ribosomal protein L21 [Odontella sinensis]
Borrelia burgdorferi - Putat 90194 gil1652022 C	1665	1652349	573204	45169IPO HAEIN	2	13439	93954)41116	I5189ISY HIME	1652577	1098641	339938	16189	gil142997	.1497	gil436158		07881		55055	573583	gil1573978	gil49316	79767 gil1001473 h	91806 gnllPIDlc2118 5
							Ш									705645						50587	67740		92123
1 77	1 209	1 227	1 232	1 247	1 272	1 290	1 333	1 508	1 553	1 569	1 620	1 701	1 702	1 704	1 746	1 748	1 749	1 756	1 825	1 853	1 4	1 42	1 57	1 64	1 80

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62	62	62			1					i i		1		1	1		1		i i		į.	1	1		1
- 1			62	62	62	62	62	62	62	62	62	62	62	62	62	61	[9]	19	61	[9	61	19	61		19
Borrelia burgdorferi - Putative coding regions of novel proteins similar to know proteins 06793 gil 1652679 hypothetical protein [Synechocystis sp.]	predicted 12.5Kd protein [Mycobacteriophage 15]	ribose 5-phosphate isomerase [Synechocystis sp.]	similar to APE1/LAP4, vacuolar aminopeptidase [Saccharomyces cerevisiae]	cysteinyl-tRNA synthetase [Bacillus subtilis]	similar to proofreading 3'-5' exonuclease and polymerase [Treponema pallidum]	putative orfW gene product [Clostridium acetobutylicum]	spoOJ93 gene product [Bacillus subtilis]	cheB peptide [Escherichia coli]	phosphomannose isomerase [Escherichia coli]	single-stranded-DNA-specific exonuclease (rec3) [Haemophilus influenzae]	unknown [Helicobacter pylori]	protoporphyrinogen oxidase (hemK) [Haemophilus influenzae]	hypothetical protein [Synechocystis sp.]	phosphatidate cytidylyltransferase [Synechocystis sp.]	collagenase [Clostridium perfringens]	tRNA guanine transglycosylase [Zymomonas mobilis]	adenine phosphoribosyltransferase form 1 [Triticum aestivum]		hypothetical protein [Synechocystis sp.]	endospore forming protein [Bacillus subtilis]	gene not found in Erwinia uredovora crt gene cluster; ORF6 [Erwinia herbicola]	210668 spIP37214IER GTP-BINDING PROTEIN ERA HOMOLOG. A_STRMU	possible N-terminal signal sequence; mature protein may be	membrane-anchored and start at Cys-17. 17.5% identity over 354-aa overlap with Candida pelliculosa beta-glucosidase.; putative [Bacillus subtilis]	ORFveg110 [Dictyostelium discoideum]
a burgdorferi - Pr gil 1652679	8 gil15893	gil1001678	gil529118	gil289284	352714 gil1633576	gil312380	gil40031	0.0	. 201	. <u>50</u>	gil1477770	gil1574130	gil1652444	gil1652668	Ó	gil498141	gil726305	gi 460955	gil1001126	gil143657	gil148409	spIP37214IER A_STRMU	gil438455		gil1513240
Borrelia 106793	107883	213969	253175	287274 gil	352714	422495	459582	484494	492322	644598	655063	714979 gil	719198 gil	793891	862737	54726	92174 gil	106557	112664 gil	153051	184227	210668	264062		265581
107458	107464	213238	251889	288749	349982	423190	458740	485147	491201	646727	655800	715668	718374	792941	862498	55889	92710	106820	111699	154445	185315	209790	262392		265982
101	102	226	266	299	357	443	489	511	518	685	695	758	762	837	917	46	81	8	103	157	193	223	273		277
	П			-	=					=	-		7	T			=		=	=	-		==		

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10 30	11 291935	Borrelia bur	urgdorferi - Put	regdorferi - Putative coding regions of novel proteins similar to know proteins	119	43
1 30			117322/13	Doc Transam malidum	100	27
1 322		313330 gil	0.1172245	Reco [Treponenia panidum]	01	<u>آ</u>
1 380		372392 gil	i1973332	OrfC [Bacillus subtilis]	61	38
1 408	401874	401479g	1147716	ribosomal protein L17 [Escherichia coli]	19	44
1 413			il1185286	ORF [Sulfolobus shibatae]	19	47
1 415	5 405927	L	irlA02827IR BS3F	ribosomal protein L30 - Bacillus stearothermophilus	61	31
1 417	7 406848	406435 p	406435 pirlB29102lR 5BS8F	ribosomal protein L18 - Bacillus stearothermophilus	19	44
1 441	421784		il153045	prolipoprotein signal peptidase [Staphylococcus aureus]	19	29
1 467	7 440722	441042 gil	il173128	ubiquitin-specific processing protease [Saccharomyces cerevisiae]	19	32
1 613		581547 gil1	11303756	YqbP [Bacillus subtilis]	19	38
1 615	5 584397	585476 _g	i1551522	TpN38(b) [Treponema pallidum]	19	26
I 673	3 632123	633622 gil	11143999	dnaK homologue [Borrelia burgdorferi]	19	41
1 675			11653709	lipoprotein NIpD [Synechocystis sp.]	- 19	50
1 743	8 699438		11303863	YqgP [Bacillus subtilis]	19	45
1 897		846688 gil	il1 <i>57</i> 3586	hydrolase (GB:Z33006_1) [Haemophilus influenzae]	19	43
1 938	8		11303831	YqfM [Bacillus subtilis]	19	36
1 7	10415	10627		T24A11.1 [Caenorhabditis elegans]	09	45
1 23				YqgR [Bacillus subtilis]	09	45
1 35		44267		cytidylate kinase [Methanococcus jannaschii]	09	49
1 198	192994	192053	11045801	hypothetical protein (SP:P32720) [Mycoplasma genitalium]	09	33
1 347	341167	339440 gil		phosphocarrier protein (enzyme I) [Mycoplasma capricolum]	09	37
1 369	361817	362233 gil	il1372995	OrfH [Borrelia burgdorferi]	09	37
1 409		401872 gil		RNA polymerase alpha-core-subunit [Bacillus subtilis]	09	40
1 438	420142	418793 gn 30	n]IPIDIe2768 0	UDP-N-acetylglucosamine 1-carboxyvinyltransferase [Bacillus subtilis]	09	40
1 566			11573923	prolipoprotein diacylglyceryl transferase (lgt) [Haemophilus influenzae]	09	57
1 587		559655 gill	il1335805	CD45 homolog [Heterodontus francisci]	09	56
1 589	561098	562558 _B	11653395	PET112 [Synechocystis sp.]	09	37

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47	34	33	26	38	36	38	34	30	40	38	40	33	42	41	38	36	34	35	39	40	35	39	38	38	34
09	09	9	09	09	09	09	09	09	09	59	29	59	59	59	59	59	59	59	59	29	59	59	59	59	59
feri - Putative coding regions of novel proteins similar to know proteins 1260 hypothetical protein [Synechocystis sp.]	elongation factor P [Synechococcus PCC7942]	hypothetical [Haemophilus influenzae]	mxaC gene product [Methylobacterium extorquens]	cytidylate kinase [Mycoplasma genitalium]	hypothetical [Haemophilus influenzae]	Ne2550 hypothetical protein [Bacillus subtilis]	NifS protein. [Escherichia coli]	unknown [Schistosoma mansoni]	type-I signal peptidase SpsB [Staphylococcus aureus]	ORF6 gene product [Bacillus subtilis]	DNA polymerase III subunit [Bacillus subtilis]	dipeptide transport system permease protein (dppB) [Haemophilus	phosphoglucose isomerase (AA 1-549) [Escherichia coli]	hypothetical [Haemophilus influenzae]	exodeoxyribonuclease V (recB) [Haemophilus influenzae]		ORF_f560 [Escherichia coli]	Similar to arginyl-tRNA synthetase (E. coli) [Saccharomyces cerevisiae]	alternate gene name yibD [Escherichia coli]	ORF for L15 ribosomal protein [Bacillus subtilis]	sigma factor (ntrA) (AA 1-502) [Azotobacter vinelandii]	hypothetical protein L - Bacillus subtilis (fragment)	unknown [Bacillus subtilis]	regulatory components of sensory transduction system [Synechocystis sp.]	proton glutamate symport protein [Bacillus caldotenax]
Borrelia burgdorferi - Pt 690076 gil1001260	Ц_	706626 gill 57.	735635 gill 16	786567 gil1046033	1	816105 gnllPII	829943	874110 gil1002	L	63234 gil5809			141174 gil42377	187659 gil1573129		276257 pirlD64084ID 64084	281525 gil8825	296707	324564 gil466	L	440759 gil392		463752 gil4674		496395 gil 143002
690957	691078	707879	734589	785899	812835	813727	831250	872578	882211	63629	102744	118925	139567	186577	242174	278281	280005	294923	325664	405646	439470	462064	462955	480078	497621
736	738	750	784	829	862	863	878	929	937	54	96	120	140	195	259	288	291	306	332	414	465	492	495	503	523
F		-	-		-	-			F	T	-	1	1	-	F		F				-		F	_	

36	38	32	37	37	37	34	30	37	41	41	35	31	29	22	34	35	43	34	34	42	32	41	35	38	32
59	58	58	58	28	28	58	28	58	58	28	28	28	58	58	58	58	28	28	28	58	57	57	57	57	57
gdorferi - Putative coding regions of novel proteins similar to know proteins 1685110 tetrahydrofolate dehydrogenase/cyclohydrolase [Streptococcus	pantothenate permease (panF) [Haemophilus influenzae]	YqeJ [Bacillus subtilis]	PID e2758 T06E6.f [Caenorhabditis elegans]	hypothetical [Haemophilus influenzae]	putative [Rhodobacter capsulatus]	oxygen-independent coproporphyrinogen III oxidase (hemN) [Haemophilus influenzae]	rhoptry protein [Plasmodium yoelii]	(AE000047) Mycoplasma pneumoniae, MG246 homolog, from M. genitalium [Mycoplasma pneumoniae]	NAD(P)H-dependent dihydroxyacetone-phosphate reductase [Bacillus subtilis]	helicase [Staphylococcus aureus]	hypothetical protein [Synechocystis sp.]	fliG [Treponema denticola]	alanine racemase, biosynthetic (alr) [Haemophilus influenzae]	minus strand repeat motif-containing gene [Borrelia burgdorferi]	574150 [ribosomal protein S1 (rpS1) [Haemophilus influenzae]	ORF YGR089w [Saccharomyces cerevisiae]	low Mr GTP-binding protein Rab32 [Homo sapiens]	YqfG [Bacillus subtilis]	putative [Bacillus subtilis]	putative protein highly homologous to E. coli RNase HII [Magnetospirillum sp.]	tlpC gene product [Bacillus subtilis]	lacC polypeptide (AA 1-310) [Staphylococcus aureus]	high level kasgamycin resistance [Bacillus subtilis]	early protein [Human papillomavirus type 19]	NAD synthetase [Rhodobacter capsulatus]
Borrelia burgdorferi - Put 886019 gil1685110	48951 gil1574003	89534 gil1303791		173009 gil1573163	189634 gil1066850	214563 gil1573441	241873 gil1041785		534750 gil974332	559370 gil153062	592435 gil1653618		749508 gil1574412		788225 gill 574150		834520 gil1575792	<u> </u>	862875 gil 1256625	[lig	187702 gil496484	248192 gil46605	gil	358495 gil396943	378025 gil45986
885060	50348	90160	115845	173515	191904	215111	238952	421010	533653	557259	591542	683208	750629	778475		796255	834332	853953	863594	865297	189636	249142	300776	358725	378249
941	40	9/	116	179	197	229	257	440	557	586	623	728	962	823	830	842	883	905	616	921	196	262	311	365	386
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	31	36	29	30	33	31	36	36	36	39	33	43	36	38	28	39	26	30	35	36	29	41	38	36	40
	57	57	57	57	57	57	57	57	57	57	57	57	57	57	56	99	99	56	56	99	56	56	56	56	26
tative coding regions of novel proteins similar to know proteins	194247 gil 1592085 M. jannaschii predicted coding region MJ1437 [Methanococcus jannaschii]	GTP-binding protein [Treponema pallidum]	Ribosomal Protein L10 [Bacillus subtilis]	[YqgH [Bacillus subtilis]	ORF2136 [Marchantia polymorpha]	acriflavine resistance protein (acrB) [Haemophilus influenzae]	[histidyl-tRNA synthetase [Methanococcus januaschii]	elongation factor Ts [Chlamydia trachomatis]	hypothetical [Haemophilus influenzae]	50S ribosomal subunit protein L9 [Escherichia coli]	replicative DNA helicase [Synechocystis sp.]	acetyl coenzyme A acetyltransferase (thiolase) (fadA) homolog - Haemophilus influenzae (strain Rd KW20)	M. jannaschii predicted coding region MJ0798 [Methanococcus jannaschii]	ORF4 [Bacillus subtilis]	phospholipase C (EC 3.1.4.3) precursor - Clostridium bifermentans	exonuclease SbcD [Escherichia coli]	probable com101A gene [Haemophilus influenzae]	large tegument protein [Human herpesvirus 7]		NADH oxidase [Serpulina hyodysenteriae]	M. jannaschii predicted coding region MJ0240 [Methanococcus jannaschii]	aminodeoxychorismate lyase (pabC) [Haemophilus influenzae]	[xylose repressor [Bacillus subtilis]	red alga1 chloroplast [Plasmodium falciparum]	UDP-N-acetylmuramoylalanine-D-glutamate ligase (murD) [Haemophilus influenzae]
Borrelia burgdorferi - Pu	394247 gil 1592085	396193 gill 732241		_		gill	778244 gil 1591660	llig	793038 gil1573941	799670 gil537044	801041 gil 1001271	803742 pirlA64092IA 64092	806952 gil1499620	867809 gil1237015	pirll 305	34277 gil1657594	7.1	91480 gil1139633	113571 gnllPIDle2469	143988 gil642030	149100 gil1499018	164388 gil1573431	gil 14	300922 gnllPIDIe2202 40	306992 gil1574691
	394690	397512	504504	689992	745857	768735	776835	790907	792328	980661	899661	802510	805240	865347	17611	35530	68915	91821	113768	142606	148561	165431	Ш	301170	308362
	399	402	533	735	794	814	821	834	988	848	849	851	855	922	12	56	29	79	112	147	153	169	183	312	317
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	077	PP / 201	Borreli	a burgdorferi - Pu	Borrelia burgdorferi - Putative coding regions of novel proteins similar to know proteins		00
	440	1/5075	- 1	g114	unknown [baciiius suotiiis]	20	87
1	456	432628		gil1	deoxyribodipyrimidine photolyase [Bacillus subtilis]	99	34
Ī	460	438178	437312 gil8	gil882453	ORF_f286; alternate name yggB; orf4 of X14436 [Escherichia	56	31
					[coli]		
	469	441309	443438	gill	NaH-antiporter protein [Enterococcus hirae]	99	32
1	809	574772	574951	gill	NADH dehydrogenase subunit 2 [Paramecium aurelia]	56	37
1	669	659498		gill	OrfH [Borrelia burgdorferi]	99	24
1	757	713509		gil8	F31D5.5 gene product [Caenorhabditis elegans]	99	40
T	791	741305	742837	gil1651873	[4-alpha-glucanotransferase [Synechocystis sp.]	99	43
1	822	779478	778291		M. jannaschii predicted coding region MJ1428 [Methanococcus	99	28
	220	733200	00000	2:11740500	January Contract Cont		r, c
	706	000106	706937	<u>g</u> 111	phosphate uridylyltransferase, SWISS-PROT Accession Number	00	3/
					[P32861 [Schizosaccharomyces pombe]		
1	39	48953	48048		hypothetical protein (SP:P23851) [Mycoplasma genitalium]	55	41
I	131	132989	131967	gil1574007	nitrogen fixation nifR3 protein (nifR3) (PIR:S49971)	55	39
		-			[Haemophilus influenzae]		
1	152	148506		gil1653100	Na+ -ATPase subunit J [Synechocystis sp.]	55	31
1	359	352690	353313 gill	gil1213334	OrfX; hypothetical 22.5 KD protein downstream of type IV	55	33
					prepilin leader peptidase gene; Method: conceptual translation supplied by author [Vibrio vulnificus]		
	361	355510	354140	gil882698	L-fuculose kinase [Escherichia coli]	55	44
1	515	488398	487652	gil397486	endonuclease G [Bos taurus]	55	33
1	551	526427	525285	gil558266	orf gene product [Wolinella succinogenes]	55	30
I	270	543745	544482 gill	gil1303811	YqeU [Bacillus subtilis]	55	33
1	279	551201	551494	gil290487	50S ribosomal subunit protein L28 [Escherichia coli]	55	37
-	584	555359	256063	gil1592301	M. jannaschii predicted coding region MJ0687 [Methanococcus	55	32
					jannaschii]		
	902	665310	665936 gil4	gil4(deoxyguanosine kinase/deoxyadenosine kinase(I) subunit [Lactobacillus acidophilus]	55	38
	771	722876	723538	gil1736440	O-sialoglycoprotein endopeptidase (EC 3.4.24.57) (Glycoprotease). [Escherichia coli]	55	39
-	786	736537	737187	gil1589778	SPINDLY [Arabidopsis thaliana]	55	34

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			Borrelia burg	gdorferi - Puta	gdorferi - Putative coding regions of novel proteins similar to know proteins		
<u> </u>	810	765243	766130 gil9	984805	glycine betaine-binding protein precursor [Bacillus subtilis]	25	35
	871	823341	823790 gil	1590959	ATP synthase, subunit K [Methanococcus jannaschii]	55	34
	868	847660	849462	gil1517942	aminopeptidase P [Sus scrofa]	55	46
	924		868236 gil	gil1142660	POM1 [Plasmodium chabaudi chabaudi]	55	41
	927	870905	870039 gil5	9 gil534839	CheR [Rhizobium meliloti]	55	32
	964	904091	903900 gil3	0 gil312694	ARS-binding factor 1 [Kluyveromyces marxianus]	55	20
	33		43124 gil	46860	delta-2-isopentenyl pyrophosphate transferase [Escherichia coli]	54	31
	63	79094	74679 gil4	115736	Orf635 gene product [Euglena gracilis]	54	37
	192		Γ	9 gil151259	HMG-CoA reductase (EC 1.1.1.88) [Pseudomonas mevalonii]	54	35
	200	194105	192951	gil1045800	ribose transport system permease protein [Mycoplasma genitalium]	54	29
	224	210749	212320 gil1	591243	M. jannaschii predicted coding region MJ0539 [Methanococcus jannaschii]	54	45
,1	256	237491	238954 gnll 24	4 gnIIPIDle2450 24	PIDIe2450 unknown [Mycobacterium tuberculosis]	54	34
	260	245698	247542	574782	exodeoxyribonuclease V (recD) [Haemophilus influenzae]	54	36
	320		312133 gill	gil1209528	D,D-carboxypeptidase [Enterococcus faecalis]	54	40
	610	577096	579909 sill	499043	M. jannaschii predicted coding region MJ0263 [Methanococcus jannaschii]	54	30
	765	720685	719995	719999 gil290216	[bride of sevenless] gene product [Drosophila virilis]	54	25
	789		739996 gil4	Sgil473804	dosage-dependent dnaK suppressor protein [Escherichia coli]	54	35
	845		798366 gil	1045767	ribosomal protein S6 [Mycoplasma genitalium]	54	35
	951	894898		1303842	YqfU [Bacillus subtilis]	54	28
	98	96019	97032	105550	flagellar P-ring protein [Pseudomonas putida]	53	40
_	68		99215	gil912478	No definition line found [Escherichia coli]	53	35
	164	159533	158562	gil1499620	M. jannaschii predicted coding region MJ0798 [Methanococcus jannaschii]	53	39
Ī	250	234276	232861 gill	303989	YqkI [Bacillus subtilis]	53	28
1	278	266053	267426 gill	749686	similar to Saccharomyces cerevisiae unknown, EMBL Accession Number Z68194 [Schizosaccharomyces pombe]	53	28
	302	292150	294309	gil1015945	methyl accepting chemotaxis homolog [Treponema denticola]	53	31
	364	358298	357702 gill	499620	M. jannaschii predicted coding region MJ0798 [Methanococcus jannaschii]	53	41

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	28	33	32	35	30	26	26	34	37	24	34	25	28	26	32	47	28	27	40	35	29	30	27	33	29	30	25	29
	53	53	53	53	53	53	52	52	52	52	52	52	52	52	52	52	52	52	52	52	52	52	52	52	52	52	52	51
Putative coding regions of novel proteins similar to know proteins	orf 06111 gene product [Saccharomyces cerevisiae]	YlxH [Borrelia burgdorferi]	cell division protein J [Methanococcus jannaschii]	GlcNAc 6-P deacetylase [Vibrio furnissii]	YqhZ [Bacillus subtilis]	H. influenzae predicted coding region H11555 [Haemophilus influenzae]	hypothetical protein [Synechocystis sp.]	P35 gene product (AA I - 314) [Escherichia coli]	in [Plasm	colicin V production protein (pur regulon) (cvpA) [Haemophilus influenzae]	secA gene product [Antithamnion sp.]	hypothetical protein [Synechocystis sp.]		glutamic acid-rich protein [Plasmodium falciparum]	24K membrane protein [Pseudomonas aeruginosa]	phnP protein [Escherichia coli]	unknown [Bacillus subtilis]	hypothetical protein (GP:X91006_2) [Methanococcus jannaschii]	(AE000047) Mycoplasma pneumoniae, MG246 homolog, from M. genitalium [Mycoplasma pneumoniae]	aspartyl-tRNA synthetase (aspS) [Haemophilus influenzae]	fibronectin/fibrinogen-binding protein [Streptococcus pyogenes]	dihydroorotate dehydrogenase [Plasmodium falciparum]	S2 gene product [Borrelia burgdorferi]	SpoVD [Bacillus subtilis]	ATP synthase, subunit D [Methanococcus jannaschii]	repeat organellar protein [Plasmodium chabaudi]	putative [Bacillus subtilis]	beta subunit RNA polymerase [Plasmodium falciparum]
		4			5	6	9		∞	9		2	551							7			6		8		5 1	
Borrelia burgdorferi	gi1940842	540684 gill 16525	gil159202	gil173220	gil130391	4 gil1574399	gil165268	gil42219	gil1151115	102746 gil157413	116879 gil288998	gil165260	gnIIPIDle 28	346532 gil160299	361800 gil216861	367695 gil 147213	372412 gil467459	416768 gil1591425	420166 gil167417	gil157328	553802 gil496254		750674 gil106341	\sim	821516 gil159229	838106 gil115115		gil587604
Borrelia	486888	540684	591032	758537	805298	834944	56944	62383	65665	102746	116879	208446	272764	346532	361800	367695	372412	416768	420166	443798	553802	715610	750674	774852	821516	838106	862110	81610
	486253	541832	590418	759748	804825	835705	58236	63264	66168	102255	115800	208898	274152	344946	361087	368462	373209	418141	420801	443436	555235	715852	751384	89/9//	820887	839581	862856	83112
	514	267	621	805	854	884	48	53	56	95	117	220	285	352	368	376	381	437	439	474	583	759	197	820	698	888	916	29
			1	-	-	=-	十	F	-		-	=		 -	F	-	1	-		1	 -	=	1	1	-	1	1	=

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	56	29	33	27	29	59	790	32	29	25	35	53	32	82	33	30	29	32	31	39	30	20	21	29	23	28	25
	51	51	51	51	51	51	51	50	50	50	50	50	50	50	50	50	50	50	50	50	50	49	48	48	48	48	48
utative coding regions of novel proteins similar to know proteins	orf4 [Bacillus subtilis]	3-hydroxy-3-methylglutaryl-CoA synthase [Gallus gallus]	ORF2 [Bacillus subtilis]	protein antigen LmSTI1 [Leishmania major]	chromate resistance protein A [Methanococcus jannaschii]		a negative regulator of nho regulan [Peaudomonas agriginosa]	ORFO [Salmonella tvnhimirium]	phospho-N-acetylmuramoyl-pentapeptide- transferase [Bacillus subtilis]	RING-finger protein [Helicoverpa armigera nucleopolyhedrovirus]	PgsA [Bacillus subtilis]	YqfV [Bacillus subtilis]	7 unknown [Mycobacterium tuberculosis]	peptidase D [Escherichia coli]	ComE [Synechocystis sp.]	frameshift [Plasmodium falciparum]	beta-galactosidase [Thermoanaerobacterium thermosulfurigenes]	B.subtilis genes rpmH, rnpA, 50kd, gidA and gidB [Bacillus subtilis]	CG Site No. 29739 [Escherichia coli]	[T03G11.2 gene product [Caenorhabditis elegans]	murE gene product [Bacillus subtilis]	involucrin [Saguinus oedipus]	ORF2 [Salmonella typhimurium]	yejE [Escherichia coli]	putative [Bacillus subtilis]	[FemA [Staphylococcus simulans]	hypothetical protein [Synechocystis sp.]
Borrelia burgdorferi - Pu	146360 gil520844	185275 gil211931	289676 gil142833	362874 gil1698880	439497 gil1591434	774842 gnilPIDIe2390	3/ 860055 3/	54067 mil5053578	102261 gil39995	117096 gill 762996	150506 gil893358	224744 gil1303843	gnIIPIDIe276 78	274710 gil147140	300778 gil1652202	\mathbb{S}	434509 gil144839	447948 gil580905	641039 gil882579	690400 gil1086864	709662 gil40162	354157 gil343314	53216 gil505363	120774 gil405908	156653 gil143213	306995 gil1762962	437315 gil1001478
	147190	186516	288759	362209	438943	772935	720030	777750	101155	118397	151159	224187	265044	276164	299525	342477	435120	448691	640194	690152	708130	353288	54046	119896	157504	305940	436152
	150	194	300	371	464	819	700	727	94	118	155	239	274	287	310	349	457	479	089	737	752	360	44	122	191	316	459

-	869	197965	Borrelia burgdorferi - P	dorferi - Putative coding regions of novel proteins similar to know proteins 56218 Dutative [Caenorhabditis elegans]	84	32
	694	690559		dedA protein (dedA) [Haemophilus influenzae]	48	22
	731	686392	686129 gil915207	gastric mucin [Sus scrofa]	48	27
-	893	844951	gnll 45	PIDIe2202 frameshift [Plasmodium falciparum]	4 8	32
	69	74673	72196 gil1766042	outer membrane protein [Neisseria gonorrhoeae]	47	30
	103	107896	108780 gill	P24A protein (unknown function) (Swiss Prot. accession number P32802) (Saccharomyces cerevisiae)	47	27
	187	181111	180215 gi 1184118	mevalonate kinase [Methanobacterium thermoautotrophicum]	47	30
	204	195930	gill	phosphoglycolate phosphatase, chromosomal (SP:P40852) [Haemophilus influenzae]	47	21
	265	251835	251098 gill 209847	repeat motif-containing gene [Borrelia burgdorferi]	47	30
	334	325837	1	uridylate kinase [Methanococcus jannaschii]	47	26
	356	349581	349991 gil849173	Probable essential component of the nucleoskeleton (Swiss Prot. accession number P32380) [Saccharomyces cerevisiae]	47	27
	490	460559	459834 gill 592264	type I restriction enzyme [Methanococcus jannaschii]	47	34
	526	499992	1	ankyrin 3 [Mus musculus]	47	29
	577	549541	548390 gnll	PIDIe2202 frameshift [Plasmodium falciparum]	47	27
	744	701189	699441 gnllPIDIe160 36	PIDIe1604 orfA gene product [Borrelia burgdorferi]	47	23
	755	713050	1	710765 pirlS41649IS4 DNA polymerase - Plasmodium falciparum	47	22
	761	717229	1	M. jannaschii predicted coding region MJ1428 [Methanococcus jannaschii]	47	37
	813	767745	768737		47	23
	824	779587	780546 gil687844	contains TPR domain-like repeats [Caenorhabditis elegans]	47	78
	881	834283	833015 gil1574393	H. influenzae predicted coding region H11548 [Haemophilus influenzae]	47	24
	988	837236	836199 gil887563	serine/threonine-protein kinase [Plasmodium falciparum]	47	30
	47	57001	55880 gil1652686	hypothetical protein [Synechocystis sp.]	46	23
	160	156659	156171 gill	ORF4 protein (AA 1-156) [Paramecium aurelia]	46	20

											80										
28	20	18	27	21	28		29	32	29	19	26	29	<u> </u>	27	23	23	26	26	31	25	19
46	46	46	46	46	46		46	46	46	46	46	46		45	45	45	4	4	44	44	43
orferi - Putative coding regions of novel proteins similar to know proteins 42681 Lpp38 [Pasteurella haemolytica]	9 NADH dehydrogenase, subunit 2 [Acanthamoeba castellanii]	6 rhoptry protein [Plasmodium yoelii]	98 hypothetical protein (GP:U19364_6) [Methanococcus jannaschii]	429375 pirlS41649IS4 DNA polymerase - Plasmodium falciparum 1649	128 Four tandem repeats of a DNA-binding domain known as the AT-lhook are found at the carboxy terminus of CarD. This protein has	been purified and found to bind in vitro to a promoter region [Myxococcus xanthus]	[Dle3332 ND5 protein [Ascaris suum]	71 apolipoprotein N-acyltransferase (cute) [Haemophilus influenzae]	5 [TpN50 precursor [Treponema pallidum]	37 outer membrane integrity protein (tolA) [Haemophilus influenzae]			aa overlap with Candida pelliculosa beta-glucosidase.; putative [Bacillus subtilis]	8 open reading frame [Mus musculus]		43 M. jannaschii predicted coding region MJ0263 [Methanococcus jannaschii]			IDle2364 F54G8.4 [Caenorhabditis elegans]	[Die2202 frameshift [Plasmodium falciparum]	99 YqeN [Bacillus subtilis]
a burgdorferi	3 gil562039	3 gil457 146	7 gil1591598	5 pirlS41649 1649	545596 gil1022328		gnIIP 9	Jgil1573271	8 gil458015	7 gil 1574537	l gil806562	909948 gil438455		5 gil220578	gil687689	gil1499043	98756 gil303895	3 gil 143245	gnllPIDle2 83	gnllPIDle2 45	gil1303799
Borrelia burgdo 232829 gill 14	32283	32730.	421747 gill59	42937;	54559(587865	666710	740008 gil45	841147 gil 15	852741 gil80	90994		198516 gil220	438949 gil68	695295 gil 149	9875(234343	670430 gnllPI 83	801045 gnllPII 45	435118
231765	323695	329090	422511	428632	545081		586903	668290	741189	843474	853463	908917		197467	438197	698657	96166	235698	668406	802490	436119
249	329	336	442	452	573		617	708	790	892	903	896		208	462	742	06	253	709	820	458
			Ī	_							Ī								-	1	

810560 809967 pirIS 17998IS1 gene COX1 intron 4 protein similar to know proteins 810560 809967 pirIS 17998IS1 gene COX1 intron 4 protein - yeast (Kluyveromyces marxianus var. lactis) mitochondrion (SGC2) 881179 879701 gil1045905 no score generated - score shown is bogus [Mycoplasma genitalium]		43 30	43 27		42 19															
Borrelia burgdorferi - Puta 810560 809967 pirlS17998IS1 7998 881179 879701 gil1045905 587863 588672 gil1045801 593472 594572 gil343962 100191 101021 gil413976 545523 546581 gallPIDIe1632 6 693458 692403 gil1151158 5792 6796 gil1256888 5792 6796 gil1256888 431037 429700 gil499647	jons of novel proteins similar to know proteins			schii	hypothetical protein (SP:P32720) [Mycoplasma genitalium]		ipa-52r gene product [Bacillus subtilis]	IIPIDIe 1632 MURF2 protein (AA 1-348) [Crithidia fasciculata]	repeat organellar protein [Plasmodium chabaudi]	Similar to chromosome segregation protein Smc1p of S. cerevisiae 4	GenBank accession number L00602), chromosome segregation	protein Cut3p of S. pombe (Swiss Prot. accession number	P41004), and C. elegans hypothetical proteins R13G10.1		neural specific DNA binding protein [Xenopus laevis]		(RL) ORF mRNA, complete cds.],	gene product [Mus musculus]	wall-associated protein [Bacillus subtilis]	repeat organellar protein [Plasmodium chahandi]
Borrelia burgdorferi - Puta 810560 809967 pirlS17998IS1 7998 881179 879701 gil1045905 587863 588672 gil1045801 593472 594572 gil343962 100191 101021 gil413976 545523 546581 gallPIDIe1632 6 693458 692403 gil1151158 5792 6796 gil1256888 5792 6796 gil1256888 431037 429700 gil499647	tive coding reg	gene COX1 var. lactis) n	no score gen genitalium]	hypothetical	hypothetical	VAR1 protei	ipa-52r gene	MURF2 pro	repeat organ	Similar to ch	(GenBank ac	protein Cut3	P41004), and	(GenBank	neural specif	hypothetical	Mus muscu	gene product	wall-associat	repeat organe
81179 881179 311250 587863 593472 100191 545523 693458 5792 5792 431037	Borrelia burgdorferi - Puta	809967 pirlS17998IS1 7998		1591425	1045801	43962	13976	546581 gnllPIDle1632	151158	256888					1150836	5			304179	905528 gill 151158
1 859 1 319 1 625 1 625 1 740 1 740 1 318 1 453 1 795		810560	881179	311250	587863					ı					214440	309735	431037		747813	907336
		1 859	1 935	1 319	1 618	1 625	1 93	1 574	1 740	1 3					1 228	1 318	1 453		1 795	1 966

Borrelia burgdorferi - Coding regions containing know proteins

Contig	Orf ID Start		Stop	match	match gene name	percent	HSP nt
110			(nt)	acession	0	ident	length
	69			85018 gblL321441	Borrelia burgdorferi peptidyl-tRNA hydrolase-	100	220
	70	86918		86340 obil 32144	Borrelia burgdorferi nentidyl-tRNA hydrolase-	100	579
)			like protein (pth) gene homologue, complete cds		
	71	87573	11698	gb L32144	Borrelia burgdorferi peptidyl-tRNA hydrolase- like protein (nth) gene homologue, complete cds	100	129
	124	123885		121759 gblM60802l	B.burgdorferei immunogen gene, 5' flank	66	2127
	126	127421		125700 emblX91965I BBATPBP	B.burgdorferi abp gene	97	284
	137	136332	139151	gblL314241	Borrelia burgdorferi (clone BbK3.11) phoA fusion protein gene, partial cds	86	248
	138	138676	138515	gblL31424	Borrelia burgdorferi (clone BbK3.11) phoA fusion protein gene, partial cds	96	09
_	165	160705	159932	gblU175911	Borrelia burgdorferi primary sigma factor (rpoD) gene, complete cds	100	774
	166	162604	i	160703 gblU175911	Borrelia burgdorferi primary sigma factor (rpoD) gene, complete cds	100	1902
	167	<u> </u>	l	162602 gblU175911	Borrelia burgdorferi primary sigma factor (rpoD) gene, complete cds	66	232
	168	164397	162811	gblU175911	Borrelia burgdorferi primary sigma factor (rpoD) gene, complete cds	66	1216
	210		199028	gbIU61498I	Borrelia burgdorferi CheA (cheA) gene, partial cds, CheW (cheW), CheX (cheX) and CheY (cheY) genes, complete cds	86	127
	211	199527	199069	199069 gblU614981	Borrelia burgdorferi CheA (cheA) gene, partial cds, CheW (cheW), CheX (cheX) and CheY (cheY) genes, complete cds	66	459
	212	200067	199549	199549 gblU61498l	Borrelia burgdorferi CheA (cheA) gene, partial cds, CheW (cheW), CheX (cheX) and CheY (cheY) genes, complete cds	66	519
_	213	201455		200046 gblU61498I	Borrelia burgdorferi CheA (cheA) gene, partial	66	1410

Borrelia burgdorferi - Coding regions containing know proteins

204115 gblU62900
gbIU62900I
emblX65139l BBHSP60
220594 emblX65139 BBHSP60
emblX54059 BBGROEL
gb1L314171
283629 emblX877251 BBDNA66K D
283683 gblM58431
gblL32146
gb U60236
gb L39965
335473 gbIU51878
338830 gbIU51878I

Borrelia burgdorferi - Coding regions containing know proteins

-	591	636	1956	424	687	144	144	956	292	1416	1220
	100	100	100	16	100	95	95	66	66	66	66
II (crr) gene, hsp90 (hptg) gene, complete cds					Borrelia burgdorferi GrpE protein homologue gene, DnaK protein homologue gene, and DnaJ protein homologue gene, complete cds's	Borrelia burgdorferi GrpE protein homologue gene, DnaK protein homologue gene, and DnaJ protein homologue gene, complete cds's	Borrelia burgdorferi GrpE protein homologue gene, DnaK protein homologue gene, and DnaJ protein homologue gene, complete cds's				Borrelia burgdorferi phenylalanyl-tRNA synthetase alpha subunit (pheS), phenylalanyl-tRNA synthetase beta subunit (pheT) and thioredoxin reductase (trxB) genes, complete cds
	338868 gblU51878	379590 gbIM96847	emblX67646 BBHSPRO	gblM97914	382617 gbIM96847	383360 gbIM96847	382688 gbIM968471	gblU82978I	384467 gbiU82978I	384733 gbiU82978I	386144 gblU82978
			381521	381943		383360	382688	383416	384467	384733	386144
	339458	378955	379566	381512	381907	382656	383005	384408	384799	386169	387733
	346	388	389	390	391	392	393	394	395	396	397
								_		-	

Borrelia burgdorferi - Coding regions containing know proteins

230	287	357	291	858	324	642
66	86 66	96	66	86	66	66
Borrelia burgdorferi phenylalanyl-tRNA synthetase alpha subunit (pheS), phenylalanyl-tRNA synthetase beta subunit (pheT) and thioredoxin reductase (trxB) genes, complete cds	B.burgdorferei promoter region DNA Borrelia burgdorferi tuf-s10 operon: elongation factor (tuf), ribosomal proteins S10 (rpsJ), L3 (rplC), L4 (rplD), L23 (rplW), L2 (rplB), S19 (rpsS), and L22 (rplV)genes, complete cds, and S3 (rpsC) gene, partial cds	Borrelia burgdorferi tuf-s10 operon: elongation factor (tuf), ribosomal proteins S10 (rpsJ), L3 (rplC), L4 (rplD), L23 (rplW), L2 (rplB), S19 (rpsS), and L22 (rplV)genes, complete cds, and S3 (rpsC) gene, partial cds	Borrelia burgdorferi tuf-s10 operon: elongation factor (tuf), ribosomal proteins S10 (rpsJ), L3 (rplC), L4 (rplD), L23 (rplW), L2 (rplB), S19 (rpsS), and L22 (rplV)genes, complete cds, and S3 (rpsC) gene, partial cds	Borrelia burgdorferi tuf-s10 operon: elongation factor (tuf), ribosomal proteins S10 (rpsJ), L3 (rplC), L4 (rplD), L23 (rplW), L2 (rplB), S19 (rpsS), and L22 (rplV)genes, complete cds, and S3 (rpsC) gene, partial cds	Borrelia burgdorferi tuf-s10 operon: elongation factor (tuf), ribosomal proteins S10 (rpsJ), L3 (rplC), L4 (rplD), L23 (rplW), L2 (rplB), S19 (rpsS), and L22 (rplV)genes, complete cds, and S3 (rpsC) gene, partial cds	Borrelia burgdorferi tuf-s10 operon: elongation factor (tuf), ribosomal proteins S10 (rpsJ), L3 (rplC), L4 (rplD), L23 (rplW), L2 (rplB), S19 (rpsS), and L22 (rplV)genes, complete cds, and
387727 gbiU82978i	407981 gblM286811 410132 gblU781931	411017 gblU781931	411386 gblU781931	gbIU781931	412529 gblU781931	412846 gblU781931
387727	407981	411017	411386	411674	412529	412846
394257	408559	411388	411676	412531	412852	413487
398	421	428	429	430	431	432
_		-	-	-		_



Borrelia burgdorferi - Coding regions containing know proteins

	633	324	1	148	171	312	180
	66	100	100	001	100	100	100
S3 (rpsC) gene, partial cds	Borrelia burgdorferi tuf-s10 operon: elongation factor (tuf), ribosomal proteins S10 (rpsJ), L3 (rplC), L4 (rplD), L23 (rplW), L2 (rplB), S19 (rpsS), and L22 (rplV)genes, complete cds, and S3 (rpsC) gene, partial cds	Borrelia burgdorferi tuf-s10 operon: elongation factor (tuf), ribosomal proteins S10 (rpsJ), L3 (rplC), L4 (rplD), L23 (rplW), L2 (rplB), S19 (rpsS), and L22 (rplV)genes, complete cds, and S3 (rpsC) gene, partial cds	Borrelia burgdorferi elongation factor EF-Tu (tuf) gene, complete cds	Borrelia burgdorferi 212 DNA gyrase b subunit (gyrB) and ribonuclease P protein component (rnpA) genes, partial cds, DnaA protein (dnaA), DNA polymerase III beta subunit (dnaN), and ribosomal protein L34 (rpmH) genes, complete cds	Borrelia burgdorferi 212 DNA gyrase b subunit (gyrB) and ribonuclease P protein component (rnpA) genes, partial cds, DnaA protein (dnaA), DNA polymerase III beta subunit (dnaN), and ribosomal protein L34 (rpmH) genes, complete cds	Borrelia burgdorferi 212 DNA gyrase b subunit (gyrB) and ribonuclease P protein component (rnpA) genes, partial cds, DnaA protein (dnaA), DNA polymerase III beta subunit (dnaN), and ribosomal protein L34 (rpmH) genes, complete cds	Borrelia burgdorferi 212 DNA gyrase b subunit (gyrB) and ribonuclease P protein component (rnpA) genes, partial cds, DnaA protein (dnaA),
	413485 gblU781931	414141 gblU781931	414503 gblL231251	450310 gblU045271	450650 gbiU045271	450897 gbIU04527i	451467 gblU045271
	413485	414141	414503	450310		450897	451467
	414117	414464	415714	450681	450820	451208	451288
	433	434	435	481	482	483	484
			_		_		1

Borrelia burgdorferi - Coding regions containing know proteins

	1170	1497	904	289	570	210	209
	66	001	86	96	100	96	66
DNA polymerase III beta subunit (dnaN), and ribosomal protein L34 (rpmH) genes, complete cds	1 485 452456 451287 gblU04527l Borrelia burgdorferi 212 DNA gyrase b subunit (gyrB) and ribonuclease P protein component (rnpA) genes, partial cds, DnaA protein (dnaA), DNA polymerase III beta subunit (dnaN), and ribosomal protein L34 (rpmH) genes, complete cds	1 486 454181 452685 gblU045271 Borrelia burgdorferi 212 DNA gyrase b subunit (gyrB) and ribonuclease P protein component (rnpA) genes, partial cds, DnaA protein (dnaA), DNA polymerase III beta subunit (dnaN), and ribosomal protein L34 (rpmH) genes, complete cds	1 487 454315 456237 gblU045271 Borrelia burgdorferi 212 DNA gyrase b subunit (gyrB) and ribonuclease P protein component (rnpA) genes, partial cds, DnaA protein (dnaA), DNA polymerase III beta subunit (dnaN), and ribosomal protein L34 (rpmH) genes, complete cds	1 488 456228 458681 emblZ12165IB B.burgdorferi gyrA gene encoding DNA gyrase BGYRAG subunit A (partial)	1 496 463825 464394 gblU03396l Borrelia burgdorferi B31 Ala-tRNA (alaT), Ile-tRNA (ileT), 16S rRNA, 23S rRNA (rrlA and rrlB), and 5S rRNA (rrfA and rrfB) genes, complete sequence	1 497 466650 466958 gblU03396l Borrelia burgdorferi B31 Ala-tRNA (alaT), Ile- tRNA (ileT), 16S rRNA, 23S rRNA (rrlA and rrlB and rrlB), and 5S rRNA (rrfA and rrfB) genes, complete sequence	1 498 467437 468033 gblU03396l Borrelia burgdorferi B31 Ala-tRNA (alaT), Ile- tRNA (ileT), 16S rRNA, 23S rRNA (rrlA and rrlB) genes,

Borrelia burgdorferi - Coding regions containing know proteins

					complete sequence		
	499	468167	<u> </u>	468433 gblÜ03396l	Borrelia burgdorferi B31 Ala-tRNA (alaT), Ile-tRNA (ileT), 16S rRNA, 23S rRNA (rrlA and rrlB), and 5S rRNA (rrfA and rrfB) genes, complete sequence	86	267
-	200	468391	468999	468999 gblU03396l	Borrelia burgdorferi B31 Ala-tRNA (alaT), Ile-tRNA (ileT), 16S rRNA, 23S rRNA (rrlA and rrlB), and 5S rRNA (rrfA and rrfB) genes, complete sequence	95	386
	501	470714	470445	470445 gblM88330l	Borrelia burgdorferi 23S ribosomal RNA gene	100	270
	502	475597		480090 gblU03396	Borrelia burgdorferi B31 Ala-tRNA (alaT), Ile-tRNA (ileT), 16S rRNA, 23S rRNA (rrlA and rrlB), and 5S rRNA (rrfA and rrfB) genes, complete sequence	26	131
	535	505532		509017 gblL484881	Borrelia burgdorferi RNA polymerase beta subunit (rpoB) gene, complete cds, RNA polymerase beta' subunit (rpoC) gene, 5' end of cds	86	2490
	536	509015	513166	513166 gblL48488l	Borrelia burgdorferi RNA polymerase beta subunit (rpoB) gene, complete cds, RNA polymerase beta' subunit (rpoC) gene, 5' end of cds	6	76
	538	513606	514106	gbIU35450I	Borrelia burgdorferi membrane protein D (bmpD) gene, complete cds	100	82
	539	514120	515229	gbIU35450I	Borrelia burgdorferi membrane protein D (bmpD) gene, complete cds	66	1110
	540	515472		516605 gblU49938I	Borrelia burgdorferi potential virulence gene cluster membrane proteins BmpC (bmpC) and BmpA (bmpA), BmpB protein (bmpB), putative protein 4, Mg ion transporter MgtE (mgtE), protein kinase C1 inhibitor PKCI (pkci) genes, complete cds	66	1134
	541	516641	517666	517666 gblL241941	Borrelia burgdorferi immunodominant antigen P39 gene, complete cds	66	1026

Borrelia burgdorferi - Coding regions containing know proteins

8 457	909 6	9 1461	1386	7 453	130	314	1404	009
86	66	66	66	100	86	66	100	100
Borrelia burgdorferi (clone pB46) membrane lipoprotein A (bmpA) gene, 3' end, membrane lipoprotein (bmpB) gene, 5' end	Borrelia burgdorferi immunodominant antigen P39 gene, complete cds	Borrelia burgdorferi potential virulence gene cluster membrane proteins BmpC (bmpC) and BmpA (bmpA), BmpB protein (bmpB), putative protein 4, Mg ion transporter MgtE (mgtE), protein kinase C1 inhibitor PKCI (pkci) genes, complete cds	Borrelia burgdorferi potential virulence gene cluster membrane proteins BmpC (bmpC) and BmpA (bmpA), BmpB protein (bmpB), putative protein 4, Mg ion transporter MgtE (mgtE), protein kinase C1 inhibitor PKCI (pkci) genes, complete cds	Borrelia burgdorferi potential virulence gene cluster membrane proteins BmpC (bmpC) and BmpA (bmpA), BmpB protein (bmpB), putative protein 4, Mg ion transporter MgtE (mgtE), protein kinase C1 inhibitor PKCI (pkci) genes, complete cds	Borrelia burgdorferi potential virulence gene cluster membrane proteins BmpC (bmpC) and BmpA (bmpA), BmpB protein (bmpB), putative protein 4, Mg ion transporter MgtE (mgtE), protein kinase C1 inhibitor PKCI (pkci) genes, complete cds	B.bergdorferi (ZS7) YSCI-like gene	B.bergdorferi (ZS7) YSC1-like gene	537144 emblX708261 B.burgdorferi gene for lipoprotein
518256 gblL35050I	518779 gblL24194l	520316 gblU49938I	521734 gblU49938I	522204 gblU49938I	522893 gbiU49938I	534772 embIX78708I BBYSC1	535058 embIX78708l BBYSC1	emb X70826
	1]	522204	522893	534772	535058	537144
517732	518168	518856	520349	521752	522168	535086	536461	536545
542	543	544	545	546	547	559	260	561
		_				-	I	

Borrelia burgdorferi - Coding regions containing know proteins

	57	786	264	56	805	84	354	1185	912	1104	750	1269	1224	969	712	561
	100	100	100	8	92	100	100	100	66	66	66	<u>00</u>	001	001	86	100
	B.burgdorferi gene for lipoprotein	Borrelia burgdorferi 22 kD antigen	Borrelia burgdorferi 22 kD antigen	Borrelia burgdorferi 22 kD antigen	Borrelia burgdorferi periplasmic substrate- binding protein homolog (p30) gene, complete cds	Borrelia burgdorferi periplasmic substrate- binding protein homolog (p30) gene, complete cds	Borrelia burgdorferi (clone Bb2.13) phoA fusion protein gene, partial cds	Borrelia burgdorferi fesmid clone 31, complete sequence	B.burgdorferi cell division genes	B.burgdorferi cell division genes	B.burgdorferi ftsW, ftsQ & ftsA genes	Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi ftsA gene, 3' end of cds, ftsZ, orf230, smf, hsIVU, flgBCE, fliEFGHI, flbABC genes, complete cds	Borrelia burgdorferi fesmid clone 31, complete sequence
BBLA7	537191 emblX70826l BBLA7	gblM90084I	537968 gblM900841	538757 gbIM90084I	572497 gbiU29143i	574204 gbiU291431	gbIL314221	597983 gblU43739I	emblX96685I BBCDG	emblX96685l BBCDG	emblX96433l BBFTSWQA	gbIU43739I	gbIU43739I	gbIU43739I	605041 gblL763031	605599 gbIU43739I
	537191	537665	237968	538757	572497	574204	586936	597983	599052	600153	600932	602173	603394	604087	605041	605509
	537652	539695	537705	538395	574092	575817	585458	596586	297967	599050	600183	506009	602171	603392	604085	602039
	262	563	564	265	909	607	616	629	630	631	632	633	634	635	636	637
		1	1	1	-		1	1	-	I	—	1	1	1		
		Ш									<u></u>					

Borrelia burgdorferi - Coding regions containing know proteins

1404	444	480	378	1770	1053	957	1332	453	630	1221	447	1350	231
97	100	100	100	100	100	100	66	66	100	66	100	100	100
606938 emblX966851 B.burgdorferi cell division genes BBCDG	Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi ftsA gene, 3' end of cds, ftsZ, orf230, smf, hsIVU, flgBCE, fliEFGHI, flbABC genes, complete cds	Borrelia burgdorferi ftsA gene, 3' end of cds, ftsZ, orf230, smf, hsIVU, flgBCE, fliEFGHI, flbABC genes, complete cds	Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi ftsA gene, 3' end of cds, ftsZ, orf230, smf, hsIVU, flgBCE, fliEFGHI, flbABC genes, complete cds	Borrelia burgdorferi ftsA gene, 3' end of cds, ftsZ, orf230, smf, hsIVU, flgBCE, fliEFGHI, flbABC genes, complete cds	Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi ftsA gene, 3' end of cds, ftsZ, orf230, smf, hsIVU, flgBCE, fliEFGHI, flbABC genes, complete cds	Borrelia burgdorferi ftsA gene, 3' end of cds, ftsZ, orf230, smf, hsIVU, flgBCE, fliEFGHI, flbABC genes, complete cds	Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi fesmid clone 31, complete sequence
emblX966851 BBCDG	607379 gblU43739l	607861 gblU43739l	608208 gblL763031	609932 gbiL763031	610982 gblU43739l	611917 gblU43739l	613246 gb L76303 	613674 gblL763031	614284 gbiU43739I	615470 gblL763031	615927 gblL763031	617260 gblU43739I	617507 gblU43739I
ļ	607379	607861	608208	609932	610982	611917	613246	613674	614284	615470	615927	617260	617507
605535	986909	607382	607831	608163	609930	610961	611915	613222	613655	614250	615481	615911	617277
638	639	640	641	642	643	644	645	646	647	648	649	650	651
_				_	-							-	-

Borrelia burgdorferi - Coding regions containing know proteins

001	1001	100	100 1	100	100	66	(E),	100	flgE), 99 813 L,	100	flgE), 100 249 L,
	Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi flagellar hook protein (flgE), flbD, flagellar motor apparatus (motAB), fliL, fliM, fliZ, flagellar export apparatus (fliPQR, flhB), flhF, flbE genes	Borrelia burgdorferi flagellar hook protein (flgE), flbD, flagellar motor apparatus (motAB), fliL, fliM, fliZ, flagellar export apparatus (fliPQR, flhB), flhF, flbE genes	Borrelia burgdorferi flagellar hook protein (flgE), flbD, flagellar motor apparatus (motAB), fliL, fliM, fliZ, flagellar export apparatus (fliPQR, flbE genes	Borrelia burgdorferi flagellar hook protein (flgE), flbD, flagellar motor apparatus (motAB), fliL, fliM, fliZ, flagellar export apparatus (fliPQR, flhB), flhF, flbE genes	Borrelia burgdorferi flagellar hook protein (flgE), flbD, flagellar motor apparatus (motAB), fliL, fliM, fliZ, flagellar export apparatus (fliPQR, flhB), flhF, flbE genes	Borrelia burgdorferi flagellar hook protein (flgE), flbD, flagellar motor apparatus (motAB), fliL,				
	619068 gblU43739l	619653 gblU43739l	620749 gblU43739l	621136 gblU43739l	621755 gblU43739l	622530 gblL759451	gblL759451	622802 gblL759451	623623 gblL759451	622819 gblL75945	623458 gblL759451
	619068	619653	620749	621136	621755	622530	621822	622802	623623	622819	623458
	618280	990619	619688	620789	621114	621742	622028	622515	622811	623007	623706
7	653	654	655	959	657	658	629	099	199	999	663
•			-				-				1

Borrelia burgdorferi - Coding regions containing know proteins

	1134	2109	1173	818	345	489	1935	286	78	2439	274	542	327	327
	66	100	100	66	100	100	100	001	100	66	100	66	100	100
fliM, fliZ, flagellar export apparatus (fliPQR, flhB), flhF, flbE genes	Borrelia burgdorferi flagellar hook protein (flgE), flbD, flagellar motor apparatus (motAB), fliL, fliM, fliZ, flagellar export apparatus (fliPQR, flhB), flhF, flbE genes	Borrelia burgdorferi flagellar hook protein (flgE), flbD, flagellar motor apparatus (motAB), fliL, fliM, fliZ, flagellar export apparatus (fliPQR, flhB), flhF, flbE genes	Borrelia burgdorferi fesmid clone 31, complete sequence	B.burgdorferei promoter element DNA	Borrelia burgdorferi (strain B31) protease (lon) gene, complete cds	Borrelia burgdorferi (strain B31) protease (lon) gene, complete cds	Borrelia burgdorferi OrfR gene, partial cds, and S20, Hbb, OrfH and Rho genes, complete cds	Borrelia burgdorferi OrfR gene, partial cds, and S20, Hbb, OrfH and Rho genes, complete cds	Borrelia burgdorferi PIG histone-like protein HBbu (hbb) gene, complete cds					
	624741 gblL759451	626843 gblL759451	628013 gbIU43739I	628912 gblU43739	628807 gbIU43739I	629398 gbIU43739I	631305 gblU43739l	631634 gblU43739l	635476 gblM286821	649420 gblL772161	649409 gblL772161	672412 gbIU35673I	672744 gblU35673I	673083 gbIU486511
			628013	628912	628807	629398	631305	631634	635476	649420	649409	672412	672744	673083
	623608	624735	626841	627998	629151	628910	629371	631314	636891	646982	651760	671567	672418	672751
	664	599	999	<i>L</i> 99	899	699	029	671	9/9	289	889	711	712	713
	_	-				I	_		-	-	-	I	I	-

Borrelia burgdorferi - Coding regions containing know proteins

4 673081 673491 gblU356731 Borrelia burgdorferi OrfR gene, partial cds, and S20, Hbb, OrfH and Rho genes, complete cds Borrelia burgdorferi OrfR gene, partial cds, and S20, Hbb, OrfH and Rho genes, complete cds S20, Hbb, OrfH and Rho genes, complete cds S20, Hbb, OrfH and Rho genes, complete cds partial cds, and S20, Hbb, OrfH and Rho genes, complete cds putative motility protein (flbF), flagellar hook associated proteins Figk (flgK) and FigL (flgL) genes, complete cds putative motility protein (flbF), flagellar hook associated proteins Figk (flgK) and FigL (flgL) genes, complete cds putative motility protein (flbF), flagellar hook associated proteins Figk (flgK) and FigL (flgL) genes, complete cds putative motility protein (flbF), flagellar hook associated proteins Figk (flgK) and FigL (flgL) genes, complete cds putative motility protein (flbF), flagellar hook associated proteins Figk (flgK) and FigL (flgL) genes, complete cds putative motility protein (flbF), flagellar hook associated proteins Figk (flgK) and FigL (flgL) genes, complete cds putative motility protein (flbF), flagellar hook associated proteins Figk (flgK) and FigL (flgL) genes, complete cds senbix956691 Borrelia burgdorferi thdF gene, partial cds, putative motility protein (flbF), flagellar hook associated proteins Figk (flgK) and FigL (flgL) genes, complete cds associated proteins Figk (flgK) and FigL (flgL) genes, complete cds associated proteins Figk (flgK) and FigL (flgL) genes, complete cds associated proteins Figk (flgK) and FigL (flgL) genes, complete cds associated proteins Figk (flgK) and FigL (flgL) genes, complete cds associated proteins Figk (flgK) and FigL (flgL) genes, complete cds associated proteins Figk (flgK) and FigL (flgL) genes, complete cds associated proteins Figk flgR) and moxR genes and DRF mygdatferi gidA, gidB and moxR genes and DRF mygdatferi gidA, gidB and moxR genes and DRF mygdatferi gidA, gidB senes and DRF mygdatferi gidA gidB senes and DRF mygdatferi gidA, gidB senes and DRF	411	1566	106			77	-	780			1841			519			1185	1893	201	301	789
4 673081 673491 gblU356731 5 673553 675118 gblU356731 6 675164 675424 gblU356731 3 724171 723770 gblU629011 4 723891 724181 gblU629011 5 725456 724164 gblU629011 727348 725441 gblU629011 727854 727336 gblU629011 BBTHDFGID 9 729284 731176 emblZ121601B BGIDAG 731149 731799 emblX956681 R	66	66	001	97		97	- ·- ·	66			66			66			86	66	00	0,6	66
4 673081 673491 gblU356731 5 673553 675118 gblU356731 6 675164 675424 gblU356731 3 724171 723770 gblU629011 4 723891 724181 gblU629011 5 727348 725441 gblU629011 7 727854 727336 gblU629011 8 727908 729308 emblX956691 BBTHDFGID 9 729284 731176 emblZ12160IB 1731149 731799 emblX956681 1731149 731799 emblX956681 173177 737848 emblX9564341	Borrelia burgdorferi OrfR gene, partial cds, and S20, Hbb, OrfH and Rho genes, complete cds	Borrelia burgdorferi OrfR gene, partial cds, and S20, Hbb, OrfH and Rho genes, complete cds	Borrelia burgdorferi OrfR gene, partial cds, and S20, Hbb, OrfH and Rho genes, complete cds	Borrelia burgdorferi thdF gene, partial cds, putative motility protein (flbF), flagellar hook associated proteins FlgK (flgK) and FlgL (flgL)	genes, complete cds	Borrelia burgdorferi thdF gene, partial cds, putative motility protein (flbF), flagellar hook	associated proteins FigK (figK) and FigL (figL) genes, complete cds	Borrelia burgdorferi thdF gene, partial cds,	associated proteins FlgK (flgK) and FlgL (flgL)	genes, complete cds	Borrelia burgdorferi thdF gene, partial cds,	putative motility protein (flbF), flagellar hook associated proteins FlgK (flgK) and FlgL (flgL)	genes, complete cds	Borrelia burgdorferi thdF gene, partial cds,	putative inounity protein (nor), magemar nook associated proteins FlgK (flgK) and FlgL (flgL)	genes, complete cds	B.burgdorferi thdF and gidA genes	B.burgdorferi thdF, gidA and gidB genes	D huradorfort wid A widD and may D sound	D.Ouiguoitett glud, glub allu illoan gelles	B.burgdorferi gidB moxR genes and ORF
5 673081 5 673533 6 675164 6 675164 7 724171 7 727348 7 727348 7 727908 7 727908 7 731777	gblU356731	gbiU35673l	gbIU356731	gbIU629011		gbIU629011	-	gbIU629011			gbIU629011			gbIU629011			emblX956691 RRTHDEGID	emblZ12160lB	OVAINA PASSONIA PASSO	BBGIDMOX R	emblX96434l
4 5 9 6 4 5 5 6	l	675118	675424	723770		724181		724164	_		725441			727336			729308	731176	721700	661161	732848
1 715 1 773 1 777 1 777 1 777 1 778 1 780	673081	673553	675164	724171		723891		725456			727348			727854			727908	729284	1-		731772
	714	715	716	773		774		775			176			777			778	779	780	00/	781
		1	_	-							=			I			1		-	-	I

Borrelia burgdorferi - Coding regions containing know proteins

	8	57	<i>L</i> 9	50	2041	158	1149	1017	1146	253	1122	476	139	75
	100	100	76	96	66	100	86	66	66	92	66	82	66	94
	B.burgdorferi gidB moxR genes and ORF	Borrelia burgdorferi phosphotransferase enzyme II (crr) gene, hsp90 (hptg) gene, complete cds	753118 gblAF003354l Borrelia burgdorferi SecA (secA) gene, complete cds	754243 gblAF003354l Borrelia burgdorferi SecA (secA) gene, complete cds		Borrelia burgdorferi SecA (secA) gene, complete cds	Borrelia burgdorferi flagellar filament cap (filD) gene, complete cds and flagellin protein (flaB) gene, partial cds	Borrelia burgdorferi gene for flagellum- associated 41kD antigen (flagellin)	B.burgdorferi DNA for hypothetical protein	B.burgdorferi DNA for hypothetical protein	Borrelia burgdorferi RecA (recA) gene, complete cds	Borrelia burgdorferi RecA (recA) gene, complete cds	Borrelia burgdorferi RecA (recA) gene, complete cds	Borrelia burgdorferi glyceraldehyde-3-phosphate dehydrogenase (GAPDH), phosphoglycerate kinase (PGK), triosephosphate isomerase (TPI)
BBGIDBMO X	733738 emblX96434l BBGIDBMO X	gbIU51878I	gblAF003354	gblAF003354	gblAF003354	gblAF0033541	761930 gblU66699l	763067 emblX16833 BBFAA	764339 emblX63898 BBHYPP	765245 emblX63898 BBHYPP	gbIU23457I	gbIU23457I	785918 gbIU23457I	857182 gbIU28760I
		751372	753118	754243	757015	757641	761930	763067	764339	765245	784400	785182	785918	857182
	732815	752154	754266	753992	754283	756991	759909	762051	763194	764337	783276	784412	785142	855179
	782	862	800	801	805	803	908	807	808	608	826	827	828	907
		Ī	1	_		1		1	1	I	I	T	I	I

Borrelia burgdorferi - Coding regions containing know proteins

	1035	1194	912	183	94	294	244	128	408	252	293
	66	66	66	6	95	65	93	96	66	100	86
genes, complete cds	Borrelia burgdorferi glyceraldehyde-3-phosphate dehydrogenase (GAPDH), phosphoglycerate kinase (PGK), triosephosphate isomerase (TPI) genes, complete cds	Borrelia burgdorferi glyceraldehyde-3-phosphate dehydrogenase (GAPDH), phosphoglycerate kinase (PGK), triosephosphate isomerase (TPI) genes, complete cds	Borrelia burgdorferi glyceraldehyde-3-phosphate dehydrogenase (GAPDH), phosphoglycerate kinase (PGK), triosephosphate isomerase (TPI) genes, complete cds	Borrelia burgdorferi sequence 3' to the triosephosphate isomerase (TPI) gene	Borrelia burgdorferi sequence 3' to the triosephosphate isomerase (TPI) gene	Borrelia burgdorferi uracil DNA glycosylase (UDG) gene, partial cds	Borrelia burgdorferi uracil DNA glycosylase (UDG) gene, partial cds	Borrelia burgdorferi uracil DNA glycosylase (UDG) gene, partial cds	Borrelia burgdorferi 1-acyl-sn-glycerol-3- phosphate acetyltransferase (plsC) gene, 3' end; topoisomerase IV beta-subunit (parE) gene, 5' end	Borrelia burgdorferi 1-acyl-sn-glycerol-3- phosphate acetyltransferase (plsC) gene, 3' end; topoisomerase IV beta-subunit (parE) gene, 5' end	B.burgdorferi ruvA, ruvB and queA genes
	858262 gbiU28760l	859463 gblU28760	860226 gblU28760	860604 gbIU576831	860316 gblU57683I	860704 gbIU57684I	gbIU57684I	gbIU57684I	874859 gblL328611	876679 gblL32861	886758 emblY088851 BBRUVABH L
	858262	859463	860226			l	861397	862113	874859	876679	886758
	857228	858270	859315	860224	860645	861447	861020	861439	874089	874877	887900
	806	606	910	911	912	913	914	915	930	931	943
									_	Annel	

Borrelia burgdorferi - Coding regions containing know proteins

909	1056	342	1320	616	324	684	6861	152	741
66	66	97	66	97	88	66	66	100	66
888570 emblY088851 B.burgdorferi ruvA, ruvB and queA genes BBRUVABH	B.burgdorferi ruvA, ruvB and queA genes	B.burgdorferi ruvA, ruvB and queA genes	B.burgdorferi pfpB gene	893909 emblY09142l B.burgdorferi yfil gene BBYFII	895371 emblX974491 B.burgdorferi priA and udk genes BBPRIAUDK	895991 emblX974491 B.burgdorferi priA and udk genes BBPRIAUDK	B.burgdorferi priA and udk genes	897963 emblX974491 B.burgdorferi pri A and udk genes BBPRIAUDK	898555 emblY091411 B.burgdorferi truA gene BBTRUA
emblY08885I BBRUVABH L	889658 emblY08885 BBRUVABH L	890271 emblY088851 BBRUVABH L	892404 emblY09140l BBPFPB	emblY09142l BBYFII	emblX97449l BBPRIAUDK	emblX97449l BBPRIAUDK	895988 emblX974491 BBPRIAUDK	emblX97449l BBPRIAUDK	emblY091411 BBTRUA
ł				893909		895991	895988	897963	898555
887965	888603	889615	890719	892893	894973	895308	976768	898577	899298
944	945	946	948	950	952	953	954	955	926

TABLE 3.Borrelia burgdorferi - Putative coding regions of novel proteins not similar to know proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)
1	1	2330	1134
1	2	3317	2934
1	8	11375	13021
1	9	11673	11386
1	10	12925	13629
1	11	13538	14146
1	17	25212	24700
1	18	25782	25357
1	19	26115	25870
1	21	27308	27051
1	22	29628	30458
1	29	40696	41217
1	30	41201	41992
1	31	42542	41985
1	32	42593	42982
1	34	44234	44031
1	38	48041	47079
1	41	49318	49617
1	43	53234	51810
1	50	59737	58208
1	58	68227	67733
1	65	79757	80404
1	66	81516	80401
1	75	89552	88353
1	82	93338	92766
1	85	95207	95854
1	104	108788	108621
1	105	109764	108943
1	108	112003	111599
1	113	114317	115846
1	114	114522	114316
1	119	118439	118927
1	121	119802	119599
1	125	125688	123967
1	129 135	128594	129235
1	136	136116 136558	135259
1	130	130338	136298
1	139		139559 140121
1	141	140573 141738	
1	143	141738	141412 142060
$\frac{1}{1}$	145	142218	142060
1	154	142686	
1	154	153832	149074 153981
$\frac{1}{1}$		158277	158474
<u> </u>	103	138211	1384/4

Borrelia burgdorferi - Putative coding regions of novel proteins not similar to know proteins

1	171	168052	166205
1	176	171592	171038
1	186	179607	180089
1	189	182345	182046
1	191	182567	182773
1	199	192561	192716
1	205	196592	197476
1	218	207717	206752
1	219	207733	208437
1	221	209337	208915
1	222	209712	209335
1	231	217179	216025
1	238	223660	223418
1	240	224720	225724
1	242	227006	227275
1	248	231761	231501
1	251	232973	233308
1	252	233669	234004
1	254	235115	235456
1	258	241824	242198
1.	261	248009	247773
1	269	256846	255872
1	276	265430	265158
1	279	266582	266298
1	281	268474	268280
1	286	274157	274384
1	292	280495	280274
1	294	281344	281042
1	298	287276	285714
1	303	292943	292644
1	304	293273	293037
1	305	294965	294648
1	308	299427	298699
1	309	299051	299212
1	326	320375	319785
1	327	320425	321036
1	331	324198	324413
1	339	332785	332459
1	341	333503	334138
1	342	334116	334739
1	343	334880	335446
1	350	342916	342443
1	351	344789	342897
1	363	357596	356931
1	367	361065	360859
1	370	362519	362196
			202170

Borrelia burgdorferi - Putative coding regions of novel proteins not similar to know proteins

1	- ' '	366905	366114
1		368632	369537
1	1	369928	370560
1	L	370532	371353
1	1	375028	373193
1	383	375102	375542
1	387	378677	378198
1	400	394952	394722
1	401	396247	394937
1	403	397569	398327
1	406	399103	399294
1	436	416160	416570
1	445	424660	423950
1	446	425181	424642
1	450	428559	428200
1	451	428933	428619
1	455	432590	431628
1	461	437823	438092
1	463	438690	438313
1	466	440749	440222
1	470	441568	441350
1	471	442039	441614
1	472	442216	442037
1	473	442666	442262
1	476	445202	445017
1	493	462106	462519
1	494	462893	462549
1	504	482111	481035
1	505	481552	481800
1	509	483249	483668
1	512	484864	485157
1	516	489171	488527
1	519	492989	492375
1	520	493626	492997
1	521	494169	494864
1	524	497185	497385
1	525	497674	499254
1	527	500251	501294
1	528	501281	502156
1	558	533912	533667
1	568	541267	541491
1	571	544436	544257
1	572	544565	545068
1	578	549603	551198
1	580	551508	551657
1	581	552337	551513
^	201	332337	221213

Borrelia burgdorferi - Putative coding regions of novel proteins not similar to know proteins

	т	T	
]			557271
1			561139
1		561825	561520
1		562536	563360
1			566519
1		568389	568682
1	1	568680	568856
1		570829	571167
1	<u> </u>	576170	577093
1		581549	581091
1	614	582910	584013
1	1	589384	588674
1		592665	593465
1	626	594542	595405
1	672	631642	632175
1	677	636650	636892
1	678	637059	638078
1	681	640861	640412
1	686	644887	645207
1	689	649716	649961
1	690	650436	650735
1	691	650733	651056
1	693	653303	653689
1	705	664733	664918
1	707	665979	666770
1	718	679155	678391
1	721	680664	681047
1	722	681523	681849
1	724	681809	682171
1	727	682853	683272
1	734	687648	688067
1	739	691613	692290
1	751	707290	707718
1	763	719197	718904
1	764	720030	719257
1	769	722198	722482
1	783	733736	734647
1	785	735554	736618
1	787	737124	739184
1	792	742924	744801
1	799	753128	752655
1	811	766129	765980
1.	812	766438	767772
1	815	770062	769790
1	818	771890	772282
1	831	788219	788836

Borrelia burgdorferi - Putative coding regions of novel proteins not similar to know proteins

1		788824	789615
1			793414
1		794295	794119
1	844	796774	796586
1	852	803096	802908
1	858	809371	809970
1	864	816108	816497
1	865	816672	817283
1	866	817281	817838
1	872	823841	824836
1	876	828191	828739
1	877	828749	829147
1	879	831328	831714
1	880	831698	833005
1	885	836201	835677
1	890	841171	840590
1	891	840594	840860
1	899	849453	850148
1	902	851608	852687
1	918	862867	863109
1	920	864292	864705
1	923	865660	865346
1	925	868212	869273
1	928	871012	872580
1	933	878576	879166
1	939	884338	883268
1	940	884999	884325
1	949	892388	892924
1	957	900141	899296
1	958	900534	900139
1	959	901526	900510
1	962	902383	903258

Borrelia burgdorferi - Putative coding regions of novel proteins similar to know proteins

TABLE 4.

Contig ORF ID Start		Stop (nt)	t) match	match gene name	% sim	1 ident
(nt)			acession	D		יים וחבווו
		7	4 gil 146582	beta-lactamase [Escherichia coli]	100	86
2 692		74	240 gil344797	galactosidase fusion protein [unidentified]	001	
3 1575			8 gil458219	ORF 4 [Borrelia burgdorferi]	94	
		414	41459 gil47453	ribosomal protein S12 [Streptococcus pneumoniae]	92	
20 14234		5621	51 bbs1161785	60 kda antigen [Borrelia coriaceae, C053, ATCC 4338, Peptide, 514 aal IBorrelia coriaceael	88	
5 1080		1652	2 gnllPIDle2012 (50	ORF-D gene product [Borrelia burgdorferi]	88	3 74
1 337		26	gnllPIDle1589 79	26 gnllPIDle1589 orfA gene product [Borrelia burgdorferi]	98	77
2 1421		1128	gnllPIDle1604	gnllPIDle1604 orfD gene product [Borrelia burgdorferi]	85	46
1 381		674		ORF 5 [Borrelia burgdorferi]	85	92
	<u> </u>		gil1591672	phosphate transport system ATP-binding protein [Methanococcus jannaschii]	84	
107 108403	\sim	10	gil882454	fructose 1,6-bisphosphate aldolase [Escherichia coli]	8	19
4 4059	6	1 1	4754 pirlA34520IA3 4520	29K calcium-binding protein, brain-specific - guinea pig (fragments)	81	
9 6084	₹	5791	gnilPIDle2012 49	ORF-C gene product [Borrelia burgdorferi]	8	72
52 49986	9	49600	pirlA027711R7 MCML	pirlA02771IR7 ribosomal protein L7/L12 - Micrococcus luteus MCML	80	19
1 307		3	gil1522636	M. jannaschii predicted coding region MJECS02 [Methanococcus jannaschii]	08	09
2 218	00	409	gil1752736	gene required for phosphoylation of oligosaccharides/ has high homology with YJR061w [Saccharomyces cerevisiae]	80	37
2 719	_	925	Г	CDC25 [Homo sapiens]	80	73
	<u> </u>	946	946 gil 1522636	M. jannaschii predicted coding region MJECS02	80	
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Borrelia burgdorferi - Putative coding regions of novel proteins similar to know proteins

99	69	58	57	57	09	42	09	57	52	20	55	58	36	56	50	55	
6/	62	78	78	78	78	78	78	78	77	LL	77	76	19/	9/	75	75	_
glucose epimerase [Bacillus thuringiensis]	outer membrane porin protein Oms28 precursor [Borrelia burgdorferi]	ribosomal protein L11 [Thermus aquaticus	orfD gene product [Borrelia burgdorferi]	gnllPIDle2532 ORF YDL065c [Saccharomyces cerevisiae]	966 gnllPIDle2012 ORF-B gene product [Borrelia burgdorferi]	CG Site No. 29739 [Escherichia coli]	gnllPIDle2012 ORF-C gene product [Borrelia burgdorferi]	ORF YDL065c [Saccharomyces cerevisiae]	transfer RNA-Tyr synthetase [Bacillus subtilis]	cellobiose phosphotransferase enzyme II" [Bacillus stearothermophilus]	similar to dihydropryridine-sensitive I-type, skeletal muscle calcium channel alpha-1 subunit (SP:CIC1_RABIT, P07293) [Caenorhabditis elegans]	unknown [Bacillus subtilis]	(pos:59955997,aa:Met) [Bacillus subtilis]	gnllPIDle1589 orfC gene product [Borrelia burgdorferi]	6674 pirlC30010iC3 hypothetical ORF-6 protein - Sauroleishmania (0010)	H. influenzae predicted coding region HI0491 [Haemophilus influenzae]	
gnill/IDle2881 24	gil1543076	gil587583	742 gnllPIDle 1604	gnllPIDle2532	gnllPIDle2012 48	gil882579	gnIIPIDIc2012 49	742 gnllPIDle2532 11	gil143795	080 gil466474	536 gil1017809	gil467376	2 gil1065989	gnllPIDic 1589 80	pirlC30010lC3 0010	gil1573470	
108239		51218	38742	27177	2966	4943	171	742	23697	24080	536	82183	2	w	6674	32163	
10/148	4878	21661	39290	27416	2382	5107	T	503	24917	22722	889	81071	208	909	8488	31639	
100	4	55	54	46	4	5		2	30	34		91	1	_	6	37	
7	8	7	4	2	7	19	78	105	2	9	∞	3	11	89	7	7	

Borrelia burgdorferi - Putative coding regions of novel proteins similar to know proteins

62	09	37	55	42	58	57	52	49	56	59	58	53	52	47	54	26	63	53	40
75	75	75	75	75	75	74	74	74	74	74	74	73	73	73	73	73	73	. 73	73
protein p23 [Borrelia burgdorferi]	2 ORF-C gene product [Borrelia burgdorferi]	2 ORF-C gene product [Borrelia burgdorferi]	ORF 2 [Borrelia burgdorferi]	unknown [Borrelia burgdorferi]	4 orfA gene product [Borrelia burgdorferi]	S-adenosylmethionine synthetase [Staphylococcus aureus]	aspartyl-tRNA synthetase [Thermus aquaticus thermophilus]	hypothetical protein [Synechocystis sp.]	974 gnllPIDle1589 orfA gene product [Borrelia burgdorferi]	gnllPIDle1589 orfC gene product [Borrelia burgdorferi]	CdsK [Borrelia burgdorferi]	glycoprotein 120 [Simian immunodeficiency virus]	hemolysin [Serpulina hyodysenteriae]	type-I signal peptidase SpsB [Staphylococcus aureus]	4 unknown [Mycobacterium tuberculosis]	Similar to Seryl-tRNA synthetase [Saccharomyces cerevisiae]	6 ORF YGR248w [Saccharomyces cerevisiae]	NADH dehydrogenase, subunit 5 [Acanthamoeba castellanii]	emml gene product [Streptococcus pyogenes]
414 gil520778	gnllPIDle2012 49	gnilPIDle2012 49	gil458217	388 gil520783	gnllPIDle1604 c 36	gil1020317	gil396501	gil1651962	gnllPIDle1589 79	gnIIPIDIe 1589 84	gil1655798	gil406135	gil511145	262 gil1595810	gnllPIDle2684 56	gil500705	8 gnllPIDle2436 81	512 gil562035	079 gil694092
414	1652	62	278	388	684	31693	109871	91103	2974	1253	719	7022	21395	44262	62341	91113	93513	3512	8079
653	2437	856	1153	744	-	30506	111301	92143	4080	468	396	6810	23695	44789	64881	00868	92803	3697	8519
	3	-	3	1	<u>. </u>	36	109	101	5	2		10	29	26	73	100	106	4	6
20	70	58	89	117	130	2	7	3	20	36	42	2	2	3	3	æ.	C	4	7

Borrelia burgdorferi - Putative coding regions of novel proteins similar to know proteins	
orrelia burgdorferi - Putative coding regions of no	proteins
orrelia burgdorferi - Putative coding regions of no	to know
orrelia burgdorferi - Putative coding regions of no	similar
orrelia burgdorferi - Putative coding regions of no	proteins
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40	55	36	64	50	41	46	51	41	46	55	36	42	52	54	48	52	42	50	09	47	41	40
73[73	73	73	73	73	73	72	72	72	72	72	72	71	71	71	711	71	71	71	71	71	71
reverse gyrase [Methanococcus iannaschii]	protein p23 [Borrelia burgdorferi]	NADH dehydrogenase [Ceanothus cuneatus]	CdsC [Borrelia burgdorferi]	gnllPIDle2012 ORF-D gene product [Borrelia burgdorferi]	adhesin B precursor (fimA) [Haemophilus influenzae]	heat shock protein 70 [Sus scrofa]	sporulation protein (spoIIIE) [Haemophilus influenzae]	myosin heavy chain [Gallus gallus]	putative cellobiose phosphotransferase enzyme II' [Bacillus subtilis]	Orf1 [Borrelia hermsii]	ORF YBR257w [Saccharomyces cerevisiae]	ErpB2 [Borrelia burgdorferi]	pyruvate kinase [Bacillus stearothermophilus]	glycyl-tRNA synthetase - Thermus thermophilus	similar to multifunctional aminoacyl-tRNA synthetase, especially to the prolyl-tRNA synthetase region [Caenorhabditis elegans]	ORF1 [Synechococcus elongatus]	secretion protein SecY (AA 1-482) [Mycoplasma capricolum]	sodium-hydrogen exchange protein-beta [Oncorhynchus mykiss]	ORF 1 [Borrelia burgdorferi]	ORF 2 [Borrelia burgdorferi]	ErpD [Borrelia burgdorferi]	ORF1 [Escherichia coli]
7756 gil1500401	4438 gil520778	gil1773311	gil1655790	gnllPIDle2012 50	gil1573074	gil1978	54013 gil1574437	gil212383	799 gil895748	3600 gil 1655859	8376 gil536681	394 gil1699017	2796 gil285623	911 pirlS58522IS5 8522	684 gil459009	54275 gil217121	175 gil44228	734 gil213778	384 gil458216	392 gil458217	066 gil1373144	883 gil145280
17756	4438	6742	2587	619	382	342	54013		21799	0096	8376	394	2796	24911	58684	54275	92175	25734		2392	2066	883
17562	4280	7074	2369	176	2	26	51644	5899	22140	8812	8579	1440	1342	26272	60156	55240	92345	25567	1179	2964	984	251
16	3	6	3	7			64	9	31	8	12	2	2	31	64	99	104	43	3	4	7	_
8	14	19	25	78	108	120	<u>е</u>	5	9	8	10	45	2	2	2	3	د	5	7	20	51	54

Borrelia burgdorferi - Putative coding regions of novel proteins similar to know proteins

48	41	48	99	35	51	58	48	54	4	47	47	50	CP	46	46	47	38	26	46	42	3 12
70	70	70	0/	70	70	70	70	70	70	70	70	70	69	69	69	69	69	69	69	89	89
50538 splQ06797IRL 50S RIBOSOMAL PROTEIN L1 (BL1).	(AE000012) Mycoplasma pneumoniae, phosphocarrier protein HPr; similar to GenBank Accession Number A49683, from M. capricolum			cdc4 gene product which is essential for initiation of DNA replication in yeast [Saccharomyces generalization in yeast of the control of the	Thy1 protein [Dictyostelium discoideum]	dciAE gene product [Bacillus subtilis]	ORF 5 [Borrelia burgdorferi]	Orf2 [Borrelia hermsii]	F01G12.6 gene product [Caenorhabditis elegans]		NADH dehydrogenase (ubiquinone) (EC 1.6.5.3) chain 4 - wheat mitochondrion	1653 gnlIPIDle1604 orfD gene product [Borrelia burgdorferi]	fructose enzyme II [Rhodobacter capsulatus]	YqgI [Bacillus subtilis]	orff; product unknown [Borrelia burgdorferi]	P30 [Borrelia burgdorferi]	protein 69 [Mycoplasma hyorhinis]			'ORF' [Escherichia coli]	adenylate kinase [Paracoccus denitrificans]
8 splQ06797IR 1_BACSU	3744 gil 1673757	2220 gil153906	73225 gnllPIDle2839 19	93273 gil836815	123 gil167913	5807 gil48808	7976 gil 1421734	5904 gil1655860	3173 gil 1255880	5237 gil1236921	3970 piriS16447IS1 6447	3 gnliPIDIe 1604 37	3860 gil151932	gil1303856	24694 gil1663561	4204 gil 16 16644	7258 gil150176	gil13233	2402 gnllPIDIe1589 79)518 gil473817	980 gil 1498049
5053	11374	222	7322	9327	12		4/9/	1590	317.	523	39 /	165	9869	98150	24697	14204	7258	8587	2402	30518	72980
51233	114025	1684	74775	93500	926	35616	48320	16458	2940	24/0	41/3	1270	65752	99712	25614	14584	7025	8414	1332	29769	72330
χ	116	4	84	107	I	4/	3 6	7	4 0	×	0	m	69	114	36	21	12	4 6	7	35	79
7	7	3	3	3	4	4 -	1 4	0 [_ 	3 5	C7	36	7	m	4	3	7 5	7 [24	7	7

Borrelia burgdorferi - Putative coding regions of novel proteins similar to know proteins

47	51	52	52			54	57	43	48	46	44	56	49	38	42	51	49	41	51	48	37		100
189	89	89	89			89	89	89	89	89	89	19	19	19	<i>L</i> 9	<i>L</i> 9	<i>L</i> 9	19		129	29		43
hypothetical [Haemophilus influenzae]	1	D9461.18p; CAI: 0.15 [Saccharomyces cerevisiae]	coded for by C. elegans cDNA CEESS55F; coded for by C. elegans cDNA vk84a1.3; coded for by C.	elegans cDNA yk78g7.3; coded for by C. elegans cDNA yk168g9.5; coded for by C. elegans cDNA	yk/8g/.5; coded for by C. elegans cDNA yk84a1.5; strong s	ORF 2 [Borrelia burgdorferi]	ORF 1 [Borrelia burgdorferi]	Orf1 [Borrelia hermsii]	Orf1 [Borrelia hermsii]	ORF 2 [Borrelia burgdorferi]	L8479.4 gene product [Saccharomyces cerevisiae]	50S ribosomal protein L33 [Synechocystis sp.]	ribosomal protein S21 [Myxococcus xanthus]	TagE [Vibrio cholerae]	unknown [Bacillus subtilis]	96502 gnllPIDle2676 alanyl-tRNA synthatase [Thermus aquaticus thermophilus]	60 kda antigen [Borrelia coriaceae, C053, ATCC 4338, Peptide, 514 aal [Borrelia coriaceae]	orfD gene product [Borrelia burgdorferi]	Orf1 [Borrelia hermsii]	SERA protein [Plasmodium falciparum]	gene required for phosphoylation of	Ongosaccharlues/ has high nomology with YJKU61w [Saccharomyces cerevisiae]	orfB gene product [Borrelia huradorferi]
385 gil1574032	gnllPIDle2551 17	gil927711	364 gil 1707057			046 gil458217	678 gil458216	gil1655859	694 gil 1655859	gil458217	133 gil577175	gil1001264	051 gil 710340	114 gil460955	gil467420	gnIIPIDle2676 07	bbs 161785	7 gnllPIDIe1604 (37	6276 gil1655859	gnllPIDle8903	5906 gil1752736		enlIPIDIe 1589
106385	68287	86074	97364			40046	40678	16520	3694	3254	133	558	54051	70114	71150	96502	31941	2967	6276	6889	2906		1817
104748	68895	88992	96519		_	40648	41916	17296	2894	3832	927	52752	54290	89069	70653	94703	30304	3590	5524	6611	4995		1221
104	78	86	111			99	57	24	5	9	7	57	62	79	81	110	42	9	6	01	9		7
7	m	3	m			4	4	9	_	29	72	7 0	2	m	m	n	4	12	12	12	17		34

Borrelia burgdorferi - Putative coding regions of novel proteins similar to know proteins

				183			
58	2	1347	796	96 vil458217	ORF 2 [Borrelia huradorferi]	27	62
2	33	28572	27751	oil340613	A 'c' was inserted after nt 360 (-nt 10/50 in	10	75
					genomic sequence (M10126)) to correct -1 frameshift probably due to gel compression [Leishmania tarentolae]	8	1
2	73	69021	80669	gil153903	methyltransferase (cheR; EC 2.1.1.24) [Salmonella typhimurium]	99	42
2	93	93739	94524	94524 gil45713	P.putida genes rpmH, rnpA, 9k, 60k, 50k, gidA, gidB, uncI and uncB [Pseudomonas putida]	99	41
8	6	6009	6902	gnIIPIDle2639 31	gnllPIDle2639 OrfD [Streptococcus pneumoniae]	99	47
4	28	20922	20665	20665 gil471731	vacuolating cytotoxin homolog [Helicobacter pylori]	99	50
4	64	47985	47107	gil1421735	ORF 6 [Borrelia burgdorferi]	99	43
9	13	7227	8591	8591 gil 1591045	hypothetical protein (SP:P31466) [Methanococcus jannaschii]	99	48
34	4	2556	3161	61 gil458218	ORF 3 [Borrelia burgdorferi]	99	42
37		982	689	89 gil974334	non-receptor tyrosine kinase [Dictyostelium discoideum]	99	55
3	17	16189	66395	95 gil1651216	Pz-peptidase [Bacillus licheniformis]	65	47
3	123	105911	104070	70 gil1575784	DNA mismatch repair protein [Aquifex pyrophilus]	65	45
9	6	5726	7126	26 gil1591045	hypothetical protein (SP:P31466) [Methanococcus jannaschii]	65	49
8	6	9684	10325	gnllPIDle2012 50	25 gnllPIDle2012 ORF-D gene product [Borrelia burgdorferi]	65	48
10	I	6	971	gil1373144	ErpD [Borrelia burgdorferi]	65	47
13	5	3956	3411	gil1209872	REV [Borrelia burgdorferi]	65	47
2	92	70509	71069	69 pirlA00547IX YEBET	protein-glutamate methylesterase (EC 3.1.1.61) - Salmonella typhimurium	64	45
3	61	48610	50838	38 gil1001335	soluble lytic transglycosylase [Synechocystis sp.]	64	42
4	5	3519	3773		M protein [Streptococcus pyogenes]	64	32
4	53	38288	37824	24 gil 1373141	ORF-10 [Borrelia burgdorferi]	64	50

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Borrelia burgdorferi - Putative coding regions of novel proteins similar to
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30	35	46	30	44	35	41	52	27	49	48	34	43	47	37	45	40	04	38	48	42	45	28
64	64	64	64	64	49	64	64	63	63	63	63	63	63	63	63	63	63	63	63	63	62	69
delta-endotoxin CrylG protoxin [Bacillus thuringiensis]	rhoptry protein [Plasmodium yoelii]	2.9-3 ORF-D [Borrelia burgdorferi]	hypothetical protein [Synechocystis sp.]	gnllPIDle2763 AARP1 protein [Plasmodium falciparum]	P35 antigen protein [Borrelia burgdorferi]	gene required for phosphoylation of oligosaccharides/ has high homology with YJR061w	kinetoplast-associated protein [Trypanosoma cruzi]	2592 gnllPIDle2362 ZK287.2 [Caenorhabditis elegans]	carboxyl-terminal protease [Synechocystis sp.]	GLUTAMYL-TRNA SYNTHETASE (EC 6.1.1.17) (GLUTAMATE-TRNA LIGASE) (GLURS).	TRAB [Plasmid pPD1]	Bts1p [Saccharomyces cerevisiae]	EC 1.1.99.5 [Mus musculus]	glycerol 3 phosphate dehydrogenase [Saccharomyces cerevisiae]	glycerol uptake facilitator [Bacillus subtilis]	ORF-D gene product [Borrelia burgdorferi]	replicative DNA helicase [Bacillus subtilis]	bifunctional protein [Methanococcus jannaschii]	adenine deaminase [Bacillus subtilis]	unknown [Borrelia burgdorferi]	phosphomannose isomerase [Escherichia coli]	cheB peptide [Escherichia coli]
5824 g1140271	gil1041785	gil1209840	gil1652934	gnllPIDle2763 80	gil1553115	788 gil1752736	gil162142	gnllPIDle2362	gil1652577	266 spiP15189ISY E_RHIME	308 gil 104 l 116	58 gil 1098641	237 gil 1339938	gil763191	gil142997	# gnllPIDle2012 (.956 gil467330	853 gil1592217	906 gil633167	268 gil520783	745 gil 146722	gil145524
5824	4499	19289	2339	839	1177	1788	2	2592	11320	26266	72308	28	71237	71349	74773	4304	24956	3853	9061	268		70573
2982	7798	19738	1608	537	308	1928	589	2837	12750	27753	71067	1056	71398	72845	75552	3747	24123	4161	9558	753	99869	69920
01	7	30	3		1	3	1	3	15	32	77	7	82	83	85	9	38	5	13	_	89	75
0	7	7	11	16	19	42	142	7	2	2	7	3	8	<i>C</i>	3	_	7	11	12	32	7	7

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36	40	37	43	36	56	375	5	36	43	36	32	41	50	45	34	44	48	50	4	38	38	
62	62	62	62	62	62	62	}	62	69	62	61	19	61	61	61	61	61	61	61	61	19	
spoOJ93 gene product [Bacillus subtilis]	single-stranded-DNA-specific exonuclease (recJ) [Haemophilus influenzae]	unknown [Helicobacter pylori]	glcB gene product [Staphylococcus carnosus]	glutamine transport ATP-binding protein Q [Methanococcus jannaschii]	CigB [Dictyostelium discoideum]	Fu=putative serine/threonine kinase [Drosophila	melanogaster, Peptide Partial Mutant, 152 aa] [Drosophila melanogaster]	ORF-A gene product [Borrelia burgdorferi]	repeat organellar protein [Plasmodium chabaudi]	gnllPIDle1539 ORF-A gene product [Borrelia burgdorferi]	ubiquitin-specific processing protease [Saccharomyces cerevisiae]	dnaK homologue [Borrelia burgdorferi]	lipoprotein NIpD [Synechocystis sp.]	YqgP [Bacillus subtilis]	ORF 7 [Borrelia burgdorferi]	CdsJ [Borrelia burgdorferi]	ORF 2 [Borrelia burgdorferi]	ORF 2 [Borrelia burgdorferi]	ORF-D gene product [Borrelia burgdorferi]	methyltransferase [Bacillus aneurinolyticus]	Similar to S. cerevisiae hypothetical protein Ykl012p	elegans hypothetical protein ZK1098.1 (Swiss Prot. accession number P34600) [Saccharomyces
5492 gil40031	5212 gill5/4144	5677 gil 1477770	104 gil1072419	5144 gil 1591493	6976 gil1513302	4378 bbsl144872		8 gnllPIDle1539 677	gil1151158	gnliPIDle1539 57	4032 gil173128	4236 gil 143999	gil1653709	gil1303863	gil1421736	gil1655797	gil458217	gil458217	gnllPIDle2012 50	gil836624	2240 gil 1066497	
95492	21766	65677	104	5144	9269	4378		538	356	629	114032	4236	6083	9261	6478	22971	8872	5551	8652	4377	2240	
96334	3/341	66414	1762	4431	6743	4563		26	586	138	114352	42737	44821	110052	47119	21496	8300	2006	9398	9079	2449	
3	ò	9/		4	8	9			2		117	55	57	125	63	35		∞	10	12	4	
7 6	n	2	0	<u>∞</u>	19	70		81	106	4	2	m	2)	m	4 (_	× ļ	77	<u>4</u>	15	<u>o</u>	

Borrelia burgdorferi - Putative coding regions of novel proteins similar to know proteins

0					cerevisiae]		
57	4	2323	1853	3 gnllPIDie 1604 37	gnllPIDle1604 orfD gene product [Borrelia burgdorferi]	61	45
50	2	1374	1156	6 gnlIPIDie2763 80	gnllPIDie2763 AARP1 protein [Plasmodium falciparum]	19	52
2	18		1536	5369 gil1573923	prolipoprotein diacylglyceryl transferase (lgt) [Haemophilus influenzae]	09	57
m	118	101571	100690	0 gil 100 1260	hypothetical protein [Synechocystis sp.]	09	47
0	120	101692	102273	3 gil1399829	elongation factor P [Synechococcus PCC7942]	9	37
9 1	32	21869	22		L-type calcium channel alpha-1 [Mus musculus]	09	50
- 0	37	23373	77	l gil458217	feri]	99	40
×	11	0/351	1385	851 gil 1065989	(pos:59955997,aa:Met) [Bacillus subtilis]	09	47
1 7	0 0	7750	1605	gi 147158	pfs [Escherichia coli]	09	51
CI		3310	2984	2984 gil153727	M protein [group G streptococcus]	109	36
/7	3	2744	3772	pirlS40422IS4 0422	772 pirlS40422IS4 hypothetical protein - Staphylococcus aureus 0422	09	31
2	62	57446	58672	58672 gil 143002	proton glutamate symport protein [Bacillus caldotenax]	59	34
2	82	74989	74051	051 gil1651878	regulatory components of sensory transduction	59	38
2	89	92119	91322	322 gil467425	unknown [Bacillus subtilis]	50	30
7	92	93010	93663	pirlA301911A3 0191	663 pirlA301911A3 hypothetical protein L - Bacillus subtilis (fragment) 0191	59	39
7	118	115604	114315		sigma factor (ntrA) (AA 1-502) [Azotobacter vinelandii]	59	35
4	41	29875	29210	gil1209831	lipoprotein [Borrelia burgdorferi]	59	34
9	4	3323	2058	058 gil624056	contains 4 ankyrin repeats; similar to D. melanogaster notch protein, Swiss-Prot Accession Number P07027 [Paramecium bursaria Chlorella virus 1]	29	37
9	25	17793	17257	7 gnllPIDle2012 48	ORF-B gene product [Borrelia burgdorferi]	59	43
						_	_

Borrelia burgdorferi - Putative coding regions of novel proteins similar to know proteins

	36	50 40		02	58 41				58 39	58 31		58 32 58 41	58 32			30							
							3	S	2 4	2 8		5				57	-		57			nz	n n
enzyme III (Strentococciis mitane)	skeletal myosin heavy chain [Thinmis thymnis]	glutamic acid-rich protein [Plasmodium falciparum]	similar to galactoside 3(4)-I-fucosyltransferase	Mag44 [Dermatonhagoides faringe]	NAD(P)H-dependent dihydroxyacetone-phosphate	reductase [Bacillus subtilis]	Hypounetical protein [Synechocystis sp.]	D35 antigen protein [Downline board of contraction of the contraction	offi: product unknown (Borrelia huradorferi)	myosin heavy chain [Sus scrofa]	Pv200 [Plasmodium vivav]			[Methanococcus jannaschii] Ribosoma Protein 1 10 [Booilloo	York [Racillus cubtilis]	M. jannaschii predicted coding region MJ0809	[Methanococcus januaschii]		P35 antigen protein [Borrelia burgdorferi]	P35 antigen protein [Borrelia burgdorferi] mature-parasite-infected erythrocyte surface antigen MESA - Plasmodium falciparium	P35 antigen protein [Borrelia burgdorferi] mature-parasite-infected erythrocyte surface antig MESA - Plasmodium falciparum P35 antigen protein [Borrelia burgdorferi]	P35 antigen protein [Borrelia burgdorferi] mature-parasite-infected erythrocyte surface antige MESA - Plasmodium falciparum P35 antigen protein [Borrelia burgdorferi] nuclear/mitotic apparatus protein [Xenopus laevis]	gil1553115 P35 antigen protein [Borrelia burgdorferi] pirlA45605lA4 mature-parasite-infected erythrocyte surface antig 5605 MESA - Plasmodium falciparum gil1553115 P35 antigen protein [Borrelia burgdorferi] gnllPIDle2614 nuclear/mitotic apparatus protein [Xenopus Jaevis 09
Seil 153677	026 gil1339977	5970 gil160299	2 gil 1055 144	8 gil1359436	7 gil974332	0 0311653610		oil1553115	238 gil1663562	gnllPIDle2647	08 68 gil457336	198 gnllPIDIe2203	gil1522636	gil786163	10 gill 303855	gil1499632		211650115	gil1553115	gil1553115 pirlA45605lA4 5605	17 gil1553115 70 pirlA45605lA4 5605 99 gil1553115		17 gil1553115 70 pirlA45605IA4 5605 99 gil1553115 18 gnllPIDle2614 09
22125	602	597	3742		20317	30/10	⊃ II ~	. 1~	24238	34904	3468	1498	247	50045	99710	26232	10111						18 9 19
22493	6241	5383	4008	835	21414	2156	93822	2423	24696	35509	3683	1941	2322	50563	100606	26564	17250	14330	2100	3183	3183	3183 7117 3027	3183 7117 3027 336
33	6	9	7		27	~	100	3	35	46		60		53	117	38		10	T	4	4 &	4 8 0	4 8 0 -
9	10	19	25	59	7	۳	3	4	4	4	15	20	55	2	3	9	~	5	111	11	11 41	11 14 15	11 14 15 17

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3 80 3 116 6 26 7 21 11 8	70112 98976	70669 gil 1372995	OrfH [Borrelia burgdorferi]	23	40
	92686				2
		99212 pirlE22845IE2		56	36
	18732	17791 gil 1655797	CdsJ (Borrelia burgdorferi)	75	11
	14706	13510 gil1574247	H. influenzae predicted coding region HI1410	36	37
53	6722	7087 gn][PIDIe2428	[Haemophilus influenzae]		7
53		76	מדווא [דמנוטרטרנוט ומרווט]	26	28
	2446	2018 gil 142 1737	ORF 8 [Borrelia burgdorferi]	75	38
61 2	712	1410 gil583161	albumin binding protein [unidentified]	95	35
	3866	3573 gil290487	50S ribosomal subunit protein L28 [Escherichia coli]	55	37
	11322	10585 gil1303811	YqeU [Bacillus subtilis]	55	33
2 34	28640	82	orf gene product [Wolinella succinogenes]	55	30
	69999	67415 gil397486	endonuclease G [Bos taurus]	55	33
3 87	75924	76550 gil403984	deoxyguanosine kinase/deoxyadenosine kinase(I)	55	38
4 66	48434	48958 gil1100900	70 kDa heat shock protein [Theileria pages]		0
140	322	68 gill 5611	gene 17, tail filter protein [Racterionhage T7]	55	32
4 34	24244	23867 gil1663563	orfIII: product unknown [Borrelia hiradorfari]	52	38
5	5510	4179 gil1513238	ORFVep 132: similar to Caeporhabditis alama ODE	7	31
			F59B10.1 encoded by EMBL Accession Number Z49132 [Dictvostelium discoideum]	4C	57
5 45	27187	25895 gnllPIDle2614 10	nuclear/mitotic apparatus protein [Xenopus laevis]	54	30
7 28	17905	18162 gil36501	C protein [Homo sapiens]	1/2	1
11 6	4415	5215 gil1707287	putative outer membrane protein [Borrelia	54	25
	1674	2501 gil392799	G5/D6 ORF [Dictyostelium discoideum]	75	30
29 5	3284	gnllPIDle1589 80	orfC gene product [Borrelia burgdorferi]	54	33
31 3	3328	4137 pirlS41649lS4	37 pirlS41649IS4 DNA polymerase - Plasmodium falciparum	27	90

Borrelia burgdorferi - Putative coding regions of novel proteins similar to know proteins

	54 36								53 28	53			53 27				52 35	50		52 26		52 35	52 52	52 52
																				, ,		S	.	5
	bud-emergence protein [Saccharomyces cerevisiae]	Rpi1p [Saccharomyces cerevisiae]	YlxH [Borrelia burgdorferi]	orf 06111 gene product [Saccharomyces cerevisiae]	cell division protein J [Methanococcus januaschii]	vacuolar aspartic proteinase precursor [Candida	EmB2 [Borrelia hirodorferi]	XLR re	T07C12.4 [Caenorhabditis elegans]	coded for by C. elegans cDNA vk54h9 5: coded for	by C. elegans cDNA yk54h9.3; similar to matrin F/G (DNA binding protein, SP-MAEG, RAT	000910) [Caenorhabditis elegans]	XLR related protein [Mus musculus]	Orf1 [Borrelia hermsii]	fibronectin/fibrinogen-binding protein	[Streptococcus pyogenes]	aspartyl-tKNA synthetase (aspS) [Haemophilus influenzae	rhoptry protein [Plasmodium voelii]	repeat organellar protein [Plasmodium chabandi]	ORF YGR023w [Saccharomyces cerevisiae]	VHB146w rene moduce 100001	NADITABLE PROUNCE (Saccharomyces cerevisiae)	macrogynus]	NADH dehydrogenase, subunit 5 [Allomyces
1049	865 gil499695	997 gil763227	3 gil 1 165254	79 gil940842	gil1592021	gil1039462	gil1699017	gil398581	gnllPIDle2483	79 gil1055100			gil398581	gil1655859	gil496254	0:11572307	10 gill 3 / 3 / 6 /	gil457146	gil1151158	8808 gnllPIDle2439 O	27 911500655	oi11736411	5.11.C.20.11.1	gil1236411
	286	99,	1438	6817	1646	14427	34152	166	8925	3679			291	2527	1265	111276	1112/0	6150	31999	18808	3499	241		322
	2560	95	13235	68814	1032	14627	34850	3672	8485	3497		į	0 1	1787	m	111638	00011	5323	32562	18485	3287	38		119
-	2	7	16	72	3	<u>~</u>	63	5	17	5		-	7	3)	-	 -		<u>∞</u>	44	29	4	2		7
	75	2	7	7	3	4 -	5	10	15	25		00	67 6	4	7	2	-	4	4	<u> </u>	25	92		84

Borrelia burgdorferi - Putative coding regions of novel proteins similar to know proteins

				Jannaschii]		
ľ	9 6362		3 gil1553115		51	26
. ¬	10 6603		7196 gnIIPIDle2563 93		51	34
	12 10333		2771 2771		51	31
	7 5919		6179 gil173241	ZIP1 protein [Saccharomyces cerevisiae]	51	38
	1 3		287 gil 1498320	cell wall-associated protease precursor [Bacillus subtilis]	51	25
11	105 106383	10712	7126 gil580905	B.subtilis genes rpmH, rnpA, 50kd, gidA and gidB	50	32
	1 1	195	5 gnllPIDle2202 01		50	38
9	62 50808	5165	gil882579	CG Site No. 29739 [Escherichia coli]	05	31
11	9 100766	01	1014 gil1086864	T03G11.2 gene product [Caenorhabditis elegans]	50	30
3	7	2	gil1663565	orfV; product unknown [Borrelia burgdorferi]	50	36
	8 4168	347(gil49402	M1.1 protein [Streptococcus pyogenes]	205	27
	7 5190	4612	gnllPIDle1589	orfE gene product [Borrelia burgdorferi]	50	28
		504	gil1553115	P35 antigen protein [Borrelia burgdorferi]	50	36
-	3 1948	1634	gnllPIDle2682 43	gnllPIDle2682 p21 [Borrelia afzelii]	50	32
	3 582	941	I gnllPIDIe2012 (ORF-D gene product [Borrelia burgdorferi]	20	40
	1 339	4	gnllPIDle2369 01	unknown [Saccharomyces cerevisiae]	20	34
	3 2001	2630	630 gil499325	STARP antigen [Plasmodium falciparum]	40	22
10		7180	180 gill 56218	putative [Caenorhabditis elegans]	48	33
75	5 65683	99059	gil1574476	dedA protein (dedA) [Haemophilus influenzae]	48	200
11,	2 97006	96743	gil915207	gastric mucin [Sus scrofa]	48	77
7	3 14743	14970	970 gil172294	protein-tyrosine phosphatase [Saccharomyces	48	33
				cievisiae		

Borrelia burgdorferi - Putative coding regions of novel proteins similar to know proteins

28	30	27	29	34	32	28			32	23	210	37	22	23	23	27	27	31	6
48	48	47	47	47	47	46			46	46	46	46	14/	45	45	45	45	44	
M. genitalium predicted coding region MG422 [Mycoplasma genitalium]	chorismate mutase subunit B [Methanococcus jannaschii]	frameshift [Plasmodium falciparum]	ankyrin 3 [Mus musculus]	type I restriction enzyme [Methanococcus januaschii]	P35 antigen protein [Borrelia burgdorferi]	Four tandem repeats of a DNA-binding domain	terminus of CarD. This protein has been purified and	Tound to bind in vitro to a promoter region [Myxococcus xanthus]	apolipoprotein N-acyltransferase (cute)	ibosomal protein S19 [Methanococcus januaschii]	glutamic acid-rich protein [Plasmodium falciparum]	241G6.i [Caenorhabditis elegans]	vicaudalD protein [Drosophila melanogaster]	M. jannaschii predicted coding region MJ0263	ntegrin homolog - yeast (Saccharomyces cerevisiae)	nknown [Saccharomyces cerevisiae]	nknown [Saccharomyces cerevisiae]	54G8.4 [Caenorhabditis elegans]	repeat organellar protein [Plasmodium chabandi]
gil1046137	gil1591322	gnIIPIDle2202 45	gil710551	gil1592264	gil1553115	gil1022328							gil157006		pirlS30782lS3 i	gnllPIDle2369	gnilPIDle2369	gnllPIDle2364 F	019 gil1151158
9293	2825	1.199	580	95240	9941	9471			77324	25719	8816	3648	15	105909	15465	4852	4	81044	5019
7980	2628	5526	55075	94515	9057	9866			78904	24361	9895	3412	632	09271	14212	3950	258	79020	4075
=	4	<u></u>	09	94	11	12				36	13	4	-	124 1	17	4		90	1
=	28	7	2	7	4	.7			m	9	10	13	138	m	4	23	92	2	121
	11 7980 9293 gil1046137 M. genitalium predicted coding region MG422 48 [Mycoplasma genitalium]	11 7980 9293 gil 1046137 M. genitalium predicted coding region MG422 48 [Mycoplasma genitalium] 4 2628 2825 gil 1591322 chorismate mutase subunit B [Methanococcus 48]	11 7980 9293 gil1046137 M. genitalium predicted coding region MG422 48 4 2628 2825 gil1591322 chorismate mutase subunit B [Methanococcus jannaschii] 48 8 5526 6677 gnllPIDle2202 frameshift [Plasmodium falciparum] 47	11 7980 9293 gil1046137 M. genitalium predicted coding region MG422 48 4 2628 2825 gil1591322 chorismate mutase subunit B [Methanococcus jannaschii] 48 8 5526 6677 gnllPIDle2202 frameshift [Plasmodium falciparum] 47 60 55075 55803 gil710551 ankyrin 3 [Mus musculus] 47	11 7980 9293 gil1046137 M. genitalium predicted coding region MG422 48 4 2628 2825 gil1591322 chorismate mutase subunit B [Methanococcus jannaschii] 48 8 5526 6677 gnllPIDle2202 frameshift [Plasmodium falciparum] 47 60 55075 55803 gil710551 ankyrin 3 [Mus musculus] 47 94 94515 95240 gil1592264 type I restriction enzyme [Methanococcus jannaschii] 47	11 7980 9293 gil1046137 M. genitalium predicted coding region MG422 48 4 2628 2825 gil1591322 chorismate mutase subunit B [Methanococcus jannaschii] 48 8 5526 6677 gnllPIDle2202 frameshift [Plasmodium falciparum] 47 60 55075 55803 gil710551 ankyrin 3 [Mus musculus] 47 94 94515 95240 gil1592264 type I restriction enzyme [Methanococcus jannaschiii] 47 11 9057 9941 gil1553115 P35 antigen protein [Borrelia burgdorferi] 47	11 7980 9293 gil1046137 M. genitalium predicted coding region MG422 48 4 2628 2825 gil1591322 chorismate mutase subunit B [Methanococcus] 48 8 5526 6677 gnllPIDle2202 frameshift [Plasmodium falciparum] 47 60 55075 55803 gil710551 ankyrin 3 [Mus musculus] 47 94 94515 95240 gil1592264 type I restriction enzyme [Methanococcus jannaschii] 47 11 9057 9941 gil1553115 P35 antigen protein [Borrelia burgdorferi] 47 12 9986 9471 gil1022328 Four tandem repeats of a DNA-binding domain 46	11 7980 9293 gil1046137 M. genitalium predicted coding region MG422 48 4 2628 2825 gil159132 chorismate mutase subunit B [Methanococcus 48 8 5526 6677 gnllPIDle2202 frameshift [Plasmodium falciparum] 47 60 55075 55803 gil710551 ankyrin 3 [Mus musculus] 47 94 94515 95240 gil1592264 type I restriction enzyme [Methanococcus jannaschii] 47 11 9057 9941 gil1553115 P35 antigen protein [Borrelia burgdorferi] 47 12 9986 9471 gil1022328 Four tandem repeats of a DNA-binding domain 46 12 9986 9471 gil1022328 Four tandem repeats of carD. This protein has been purified and 47	11 7980 9293 gil1046137 M. genitalium predicted coding region MG422 48	11 7980 9293 gil1046137 M. genitalium predicted coding region MG422 48	11 7980 9293 gil1046137 M. genitalium predicted coding region MG422 48 2628 2825 gil1591322 chorismate mutase subunit B [Methanococcus 48 2628 2825 gil1591322 chorismate mutase subunit B [Methanococcus 48 47 45 55 6677 gnllPIDle2202 frameshift [Plasmodium falciparum] 47 49 94515 55803 gil710551 ankyrin 3 [Mus musculus] 47 40 94515 95240 gil1592264 type I restriction enzyme [Methanococcus jannaschii] 47 40 94515 9941 gil1553115 P35 antigen protein [Borrelia burgdorferi] 47 40 9471 gil1022328 Four tandem repeats of a DNA-binding domain known as the AT-hook are found at the carboxy terminus of CarD. This protein has been purified and found to bind in vitro to a promoter region [Myxococcus xanthus] Myxococcus xanthus] Haemophilus influenzae 25719 gil1592272 ribosomal protein S19 [Methanococcus iannaschii] 46 2628 2825 gil1573271 apolipoprotein N-acyltransferase (cute) 47 47 47 47 48 47 47 49 47 47 49 47 47 40 47 47 41 47 42 48 47 43 47 44 47 45 48 48 48 45 48 48 47 49 48 48 48 49 49 48 49 49 49 40 40 40 40 40 40 41 40 42 40 40 43 40 44 40 45 40 45 40 46 47 40 48 40 49 40 40 40 40 40 41 40 42 40 43 40 44 45 40 45 40 46 47 48 49 40 49 40 40 40 40 40 40 40	11 7980 9293 gil1046137 M. genitalium predicted coding region MG422 48	11 7980 9293 gil1046137 M. genitalium predicted coding region MG422 48	11 7980 9293 gil1046137 M. genitalium predicted coding region MG422 48	11 7980 9293 gill 046137 M. genitalium predicted coding region MG422 M. genitalium Mycoplasma genitalium Mycoplasma genitalium Mycoplasma genitalium Mycoplasma genitalium Mycoccus Mycoplasma genitalium Mycoccus Mycoplasma genitalium Mycoplasma genitalium Mycoccus Mycoccus Mycoplasma Myco	1 7980 9293 gill 046137 M. genitalium predicted coding region MG422 48	1980 9293 gil1046137 M. genitalium predicted coding region MG422 48	11 7986 9293 gill 046137 M. genitalium predicted coding region MG422 48	11 7980 9293 gil1046137 M. genitalium predicted coding region MG422 48

Borrelia burgdorferi - Putative coding regions of novel proteins similar to know proteins

17		3 1735		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1			
1				2771 2771	2142 pinA42//11A4 reticulocyte-binding protein 1 - Plasmodium vivax	44	26
22		7 4179		2827 oil563812	YCAD CIV.		
31		1687		211700051	ver -c [venobns raevis]	44	20
	•			2/01/gil1438931	cutinase negative acting protein [Fusarium solani f.	43	
3		7 4086		5186 gil343962	VARI protein [Candida glabrata]		
28		II		496 gil157804	laminin B7 chain [Dressentil	42	25
28	,	5 2889		1 nirl (30787163	informin De cham [D1030pmia melanogaster]	42	23
				0782	0782 Integral mornolog - yeast (Saccharomyces cerevisiae)	42	18
34		1 209		1234 gil 1655797	Ods I Borra in huma Santa		
65	(4.)	3 1035		1415 oil1654220	variable maior and supplied in the supplied of	42	27
2		9544		anlibitals 1627	Variable major protein 10 [Borrefia hermsii]	42	34
		· · ·		8 mr 10 6 10 5 2	Orong Built 1005 MORF 2 protein (AA 1-348) [Crithidia fasciculata]	41	26
3	122	104072)	3017 gil 151158	repeat Organe lar protein [Dloggedite		
18	9	5122		Γ	M issued in the contraction of t	41	20
					Methanococcus ionneced coding region MJ0797	40	20
9	9	4662		3964 gil600448	Varl profein (as 1-330) [Candida;ii:-1		
4	10	7637		T	microfilogial charther Carrolle IIIIIs	39	24
					sigmodontis 1	37	[6]
					Company of the Compan		

Borrelia burgdorferi - Coding regions containing to know proteins

TABLE 5.

_	1	Can a man	_	nt) matcn	match gene name	nercent	HCP nt
1			- 1	acession)	ident	length
2		15372	1740,	402 gblM90084l	Borrelia burgdorferi 22 kD antigen	100	
2	21		16310	310 gblM90084l	Borrelia burgdorferi 22 kD antigen	100	
2			17099	099 gblM90084l		001	6
2		17415	1787	876 emblX70826IB BLA7		100	
2		18522	17923	923 emblX70826lB BLA7	B.burgdorferi gene for lipoprotein	100	009
2	25	18606	20005	20009 emblX78708IB BYSC1	B.bergdorferi (ZS7) YSC1-like gene	100	1404
2	26	18661	20295	emblX78708IB BYSC1	295 emblX78708IB B.bergdorferi (ZS7) YSC1-like gene BYSC1	66	314
2	38	32899	32174	74 gblU49938I	Borrelia burgdorferi potential virulence gene cluster	98	130
					membrane proteins BmpC (bmpC) and BmpA (bmpA), BmpB protein (bmpB), putative protein 4, Mg ion transporter MotF (motF), protein binges C1		
					inhibitor PKCI (pkci) genes, complete cds		
2	39	33315	32863	363 gblU49938l	Borrelia burgdorferi potential virulence gene cluster	100	453
					membrane proteins BmpC (bmpC) and BmpA		
		- <u></u>			(binpA), binpb protein (binpb), putative protein 4, Mo ion transporter More (more) protein Finance C1		
					inhibitor PKCI (pkci) genes, complete cds		
7	40	34718	33333	333 gbIU49938I	Borrelia burgdorferi potential virulence gene cluster	66	1386
		_			membrane proteins BmpC (bmpC) and BmpA		
					(bmpA), BmpB protein (bmpB), putative protein 4,		
					ing ion transporter ingth (mgth.), protein kinase CI inhibitor PKCI (pkci) genes, complete cds		
2	41	36211	34751	51 gblU49938I	Borrelia burgdorferi potential virulence gene cluster	66	1461
					membrane proteins BmpC (bmpC) and BmpA		
					(bmpA), BmpB protein (bmpB), putative protein 4,		
					Mg Ion transporter Mgt (mgt), protein kinase C1 inhibitor PKCI (pkci) genes, complete cds		
2	42	36899	36288	88 gblL241941	Borrelia burgdorferi immunodominant antigen P39	06	808

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					gene complete cds		
c	77	27225	26011	-LI 250501	Bene, comprete cus		
٧	f	CCC1C	30011	30611 goll.330301	borrena burgaorreri (clone pb46) membrane lipoprotein A (bmpA) gene, 3' end, membrane lipoprotein (bmpB) gene, 5' end	86	457
2	44	38426	37401	101 gblL241941	Borrelia burgdorferi immunodominant antigen P39 gene, complete cds	66	1026
8	45	39595	38462	38462 gblU49938	Borrelia burgdorferi potential virulence gene cluster membrane proteins BmpC (bmpC) and BmpA (bmpA), BmpB protein (bmpB), putative protein 4, Mg ion transporter MgtE (mgtE), protein kinase C1 inhibitor PKCI (pkci) genes, complete cds	66	1134
2	46	40947	39838	39838 gblU35450I	Borrelia burgdorferi membrane protein D (bmpD) gene, complete cds	66	1110
2	47	41461	40961	40961 gb U35450	Borrelia burgdorferi membrane protein D (bmpD) gene, complete cds	100	82
2	49	46052	41901	41901 gblL484881	Borrelia burgdorferi RNA polymerase beta subunit (rpoB) gene, complete cds, RNA polymerase beta' subunit (rpoC) gene, 5' end of cds	97	92
2	51	49535	46050	50 gblL484881	Borrelia burgdorferi RNA polymerase beta subunit (rpoB) gene, complete cds, RNA polymerase beta' subunit (rpoC) gene, 5' end of cds	86	2490
2	83	79470	74977	77 gblU03396I	Borrelia burgdorferi B31 Ala-tRNA (alaT), Ile-tRNA (ileT), 16S rRNA, 23S rRNA (rrlA and rrlB), and 5S rRNA (rrfA and rrfB) genes, complete sequence	97	131
7	84	84351	84620	84620 gblM88330l	Borrelia burgdorferi 23S ribosomal RNA gene	100	270
7	82	86923	86066	166 gblU033961	Borrelia burgdorferi B31 Ala-tRNA (alaT), Ile-tRNA (ileT), 16S rRNA, 23S rRNA (rrlA and rrlB), and 5S rRNA (rrfA and rrfB) genes, complete sequence	95	386
2	98	87637	87041	gblU03396l	Borrelia burgdorferi B31 Ala-tRNA (alaT), Ile-tRNA (ileT), 16S rRNA, 23S rRNA (rrlA and rrlB), and 5S rRNA (rrfA and rrfB) genes, complete sequence	66	209

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2 877 88424 88116 gblU03396l Borrelia burgdorferi B31 Ala-tRNA (alaT), Ile- P6 2 88 91249 90680 gblU03396l Borrelia burgdorferi B31 Ala-tRNA (alaT), Ile- Ilo 100 2 96 98846 96393 embZ12165lB Borrelia burgdorferi B31 Ala-tRNA (alaT), Ile- Ilo 100 2 96 98846 96393 embZ12165lB Burgdorferi g1A gaee encoding DNA gyrase Complete Squence 96 2 97 100759 98837 gblU04327l Borrelia burgdorferi 212 DNA gyrase b subunit (maA), and ribosomal protein L34 (pmH) genes, complete cds subunit (dnaA), and ribosomal protein L34 (pmH) genes, complete cds ribosomal protein L34 (pmH) genes, complete cds ribosomal protein L34 (pmH) genes, complete cds protein component (mpA) genes, partial cds, DnaA protein (dnaA), DNA polymerase III bet a subunit (dnaA), and ribosomal protein L34 (pmH) genes, complete cds protein component (mpA) genes, partial cds, DnaA protein (dnaA), DNA gornelia burgdorferi 212 DNA gyrase b subunit (gyrB) and ribonuclease P protein component (mpA) genes, partial cds, DnaA protein (dnaA), DNA polymerase III beta subunit (dnaA), and ribosomal protein L34 (pmH) genes, complete cds brown and ribosomal protein E34 (pmH) genes, complete cds brown and ribosomal protein E34 (pmH) genes, complete cds gyrB and ribonuclease P protein component (mpA) genes, partial cds, DnaA protein (dnaA), DNA polymerase III beta subunit (dnaA), and ribosomal protein E34 (pmH) genes, complete cds gyrB and ribonuclease III beta subunit (dnaA), and ribosomal protein E34 (pmH) genes, complete cds gy	210	570	289	904	1497	1170	180	312
88 91249 90680 gbiU03396i 96 98846 96393 embiZ12165iB BGYRAG 97 100759 98837 gbiU04527i 98 100893 102389 gbiU04527i 100 103786 103607 gbiU04527i	96	100	96	86	100	66	001	100
88 91249 90680 gbiU03396i 96 98846 96393 embiZ12165iB BGYRAG 97 100759 98837 gbiU04527i 98 100893 102389 gbiU04527i 100 103786 103607 gbiU04527i	Sorrelia burgdorferi B31 Ala-tRNA (alaT), Ile- RNA (ileT), 16S rRNA, 23S rRNA (rrlA and rlB), and 5S rRNA (rrfA and rrfB) genes, complete sequence	Sorrelia burgdorferi B31 Ala-tRNA (alaT), Ile- RNA (ileT), 16S rRNA, 23S rRNA (rrlA and rlB), and 5S rRNA (rrfA and rrfB) genes, omplete sequence	3.burgdorferi gyrA gene encoding DNA gyrase ubunit A (partial)	Sorrelia burgdorferi 212 DNA gyrase b subunit gyrB) and ribonuclease P protein component rnpA) genes, partial cds, DnaA protein (dnaA), DNA polymerase III beta subunit (dnaN), and bosomal protein L34 (rpmH) genes, complete cds	gyrB) and ribonuclease P protein component mpA) genes, partial cds, DnaA protein (dnaA), NA polymerase III beta subunit (dnaN), and bosomal protein L34 (rpmH) genes, complete cds	orrelia burgdorferi 212 DNA gyrase b subunit gyrB) and ribonuclease P protein component npA) genes, partial cds, DnaA protein (dnaA), NA polymerase III beta subunit (dnaN), and bosomal protein L34 (rpmH) genes, complete cds	orrelia burgdorferi 212 DNA gyrase b subunit syrB) and ribonuclease P protein component inpA) genes, partial cds, DnaA protein (dnaA), NA polymerase III beta subunit (dnaN), and bosomal protein L34 (rpmH) genes, complete cds	Borrelia burgdorferi 212 DNA gyrase b subunit (gyrB) and ribonuclease P protein component (rnpA) genes, partial cds, DnaA protein (dnaA), DNA polymerase III beta subunit (dnaN), and
96 98846 97 100759 100893 1 99 102618 1								
88 96 101 100 101 101 101	88116	08906	96393	98837	102389		103607	
	88424	91249	98846	100759	100893	102618	103786	103866
7 7 7 7 7	87	88	96	97	86	66	100	101
, , , , , , , , , , , , , , , , , , , ,	2	2	2	2	2	2	2	2

Borrelia burgdorferi - Coding regions containing to know proteins

Borrelia burgdorferi - Coding regions containing to know proteins

444	480	378	1770	1053	957	1332	453	630	1221	447	1350	231	789
100	100	100	100	100	100	66	66	100	66	100	100	100	100
Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi ftsA gene, 3' end of cds, ftsZ, orf230, smf, hslVU, flgBCE, fliEFGHI, flbABC genes, complete cds	Borrelia burgdorferi ftsA gene, 3' end of cds, ftsZ, orf230, smf, hsIVU, flgBCE, fliEFGHI, flbABC genes, complete cds	Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi ftsA gene, 3' end of cds, ftsZ, orf230, smf, hsIVU, flgBCE, fliEFGHI, flbABC genes, complete cds	Borrelia burgdorferi ftsA gene, 3' end of cds, ftsZ, orf230, smf, hslVU, flgBCE, fliEFGHI, flbABC genes, complete cds	Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi ftsA gene, 3' end of cds, ftsZ, orf230, smf, hsIVU, flgBCE, fliEFGHI, flbABC genes, complete cds	Borrelia burgdorferi ftsA gene, 3' end of cds, ftsZ, orf230, smf, hslVU, flgBCE, fliEFGHI, flbABC genes, complete cds	Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi fesmid clone 31, complete sequence
993 gbIU43739I	475 gbIU43739I	gblL76303I	20546 gblL763031	596 gbIU43739 	531 gblU43739l 	860 gblL76303	288 gblL763031	898 gbIU43739I	084 gblL76303l	541 gblL76303 	874 gblU437391	121 gblU437391	900 gblU437391
17993	18475	18822	20546	21596	22531	23860	24288	24898	26084		27874	28121	28900
17550	17996	18445	18777	20544	21575	22529	23836	24269	24864	26092	26525	27891	28112
22	23	24	25	26	27	28	29	30	31	32	33	34	35
3	m	3	3	3	3	3	3	3	3	3	3	3	3

Borrelia burgdorferi - Coding regions containing to know proteins

789	588	1062	348	642	789	207	288	813	249	1134
100	100	100	100	100	66	100	100	100	100	66
Borrelia burgdorferi fesmid clone 31, complete sequence	Borrelia burgdorferi flagellar hook protein (flgE), flbD, flagellar motor apparatus (motAB), fliL, fliM, fliZ, flagellar export apparatus (fliPQR, flhB), flhE, flbE genes	Borrelia burgdorferi flagellar hook protein (flgE), flbD, flagellar motor apparatus (motAB), fliL, fliM, fliZ, flagellar export apparatus (fliPQR, flhB), flbE genes	Borrelia burgdorferi flagellar hook protein (flgE), flbD, flagellar motor apparatus (motAB), fliL, fliM, fliZ, flagellar export apparatus (fliPQR, flhB), flbE genes	Borrelia burgdorferi flagellar hook protein (flgE), flbD, flagellar motor apparatus (motAB), fliL, fliM, fliZ, flagellar export apparatus (fliPQR, flhB), flbE genes	Borrelia burgdorferi flagellar hook protein (flgE), flbD, flagellar motor apparatus (motAB), fliL, fliM, fliZ, flagellar export apparatus (fliPQR, flhB), flhF, flhF, genes	Borrelia burgdorferi flagellar hook protein (flgE), flbD, flagellar motor apparatus (motAB), fliL, fliM, fliZ, flagellar export apparatus (fliPQR, flhB), flbE genes				
682 gblU43/39	267 gblU43739I	gbIU43739I	50 gbIU43739I	69 gbIU437391	44 gblL75945l	36 gblL75945i	16 gblL759451	37 gblL759451	72 gbiL75945i	55 gblL75945l
78967	30267	31363	31750	100		32436		34237	34072	35355
78894	29680	30302	31403	31728	32356	32642	33129	33425	34320	34222
000	37	38	39	40	41	42	43	44	45	46
0	m	3	က	£ .	m	<i>w</i>	m	m	m	3

Borrelia burgdorferi - Coding regions containing to know proteins

100	11/3	918 66	100 345	100 489	100 1935	100 286	100	24	100 274	99 542	100 327	100 327	99 411	99 1566	100 106	
flbD, flagellar motor apparatus (motAB), fliL, fliM, fliZ, flagellar export apparatus (fliPQR, flhB), flhF, flbE genes	Borrelia burgdorferi fesmid clone 31, complete sequence	B.burgdorferei promoter element DNA	Borrelia burgdorferi (strain B31) protease (lon) gene, complete cds	Borrelia burgdorferi (strain B31) protease (Ion) gene, complete cds	Borrelia burgdorferi OrfR gene, partial cds, and S20, Hbb, OrfH and Rho genes, complete cds	Borrelia burgdorferi OrfR gene, partial cds, and S20, Hbb, OrfH and Rho genes, complete cds	Borrelia burgdorferi P1G histone-like protein HBbu (hbb) gene, complete cds	Borrelia burgdorferi OrfR gene, partial cds, and S20, Hbb, OrfH and Rho genes, complete cds	Borrelia burgdorferi OrfR gene, partial cds, and S20, Hbb, OrfH and Rho genes, complete cds	Borrelia burgdorferi OrfR gene, partial cds, and S20, Hbb, OrfH and Rho genes, complete cds						
100 E C	627 gblU437391	526 gblU437391	gbIU43739I	012 gb U43739	gblU43739l	gbIU43739I	gbIM28682I	60034 gblL772161	60023 gblL77216	83026 gblU356731	gblU356731	gbIU486511	05 gblU356731	32 gblU356731	38 gblU35673	
	38027	39526	39421	40012	19	42248	46090	60034	60023	83026	83358	83697	84105	85732	86038	
37, 17	3/433	38612	39765	39524	39985	41928	47505	57596	62374	82181	83032	83365	83695	84167	82778	
0	0	64	2	21	25	53	28	89	69	92	93	94	95	96	7.6	
, 6	0 6	2	2 6	20 (2	χ.	3	3	3	3		m	3	m (2	

Borrelia burgdorferi - Coding regions containing to know proteins

789	996	213	373	370	243	169	329	564	147	533	731	903	882	370	375
66	100	100	100	78	66	100	66	66	100	93	69	66	100	88	68
Borrelia burgdorferi outer membrane porin protein Oms28 precursor (oms28) gene, complete cds	Borrelia burgdorferi P35 antigen protein gene, and 7.5 kDa lipoprotein gene, complete cds	Borrelia burgdorferi strain B31 6.6 kDa lipoprotein gene, complete cds	Borrelia burgdorferi P35 antigen protein gene, and 7.5 kDa lipoprotein gene, complete cds	Borrelia burgdorferi 27kD protein antigen gene (p27), complete cds	Borrelia burgdorferi 49kb linear plasmid small 12kDa lipoprotein gene, complete cds	Borrelia burgdorferi (clone BbK2.1) phoA fusion protein gene, partial cds	Borrelia burgdorferi decorin binding protein B (DbpB) gene, complete cds	Borrelia burgdorferi decorin binding protein B (DbpB) gene, complete cds	Borrelia burgdorferi decorin binding protein B (DbpB) gene, complete cds	Borrelia burgdorferi decorin binding protein A (DbpA) gene, complete cds	Borrelia burgdorferi plasmid cp18, OspE (ospE) gene, partial cds	Borrelia burgdorferi (27985CT2) OspA gene, 3' end and OspB gene, complete cds	B.burgdorferi OspA gene and 5'flanking region	Borrelia burgdorferi outer surface protein A (ospA) and outer surface protein B (ospB) genes, complete cds	Borrelia burgdorferi outer surface protein A (ospA) and outer surface protein B (ospB) genes, complete
147 gblU61142I	gblU59487I	153 gblU59859I	.230 gbIU59487I	414 gblM85216	753 gbIU224511	793 gblL31427	gblU75867I	36929 gbIU75867I	36692 gbIU75867	624 gbIU75866I	318 gblU425991	gbIL231371	347 emblA04009lA 04009	gbIL 19702	58 gblL19702l
1147	11002		12230	13414	13753	17793	36347	36929	36692	37624	39318		43347	44403	44758
1935	10037	11365	11577	12578	13511	18668	36694	36351	36838	37001	40073	43349	44228	44792	45198
2	12	13	14	15	16	23	49	50	51	52	55	58	59	09	61
4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4

Borrelia burgdorferi - Coding regions containing to know proteins

					cds		
4	62	46440	382	7021	Borrelia burgdorferi outer surface protein A (ospA) and outer surface protein B (ospB) genes, complete cds	85	622
4	<i>L</i> 9	49363	50622 gblL34016		Borrelia burgdorferi (clone 8) S1 gene, complete cds	66	1260
4	89	50708	_		Borrelia burgdorferi (clone 8) S2 gene, complete cds	66	837
4	69	52203	51655 gblL31423		Borrelia burgdorferi (clone BbK2.14) phoA fusion protein gene, partial cds	66	292
4	70	53018	52488 gblL41151		Borrelia burgdorferi (clone 8) s3 gene, complete cds	66	297
N	1	535	71 gblU60642		Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	91	465
S	2	1526	546 gbIU60642		Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	68	374
S	4	2395	2129 gblL31425		Borrelia burgdorferi (clone BbK3.168) phoA fusion protein gene, partial cds	86	135
5		6832	6542 gblS66708		{target sequence for detection of Lyme disease agent} [Borrelia burgdorferi, B31, 30-kb circular plasmid pIP87, Plasmid, 416 nt]	76	290
5	12	7422	6817 gb U44914		Borrelia burgdorferi plasmid cp32-2, erpC and erpD genes, complete cds	87	595
2	13	8167	7565 gb U44914		Borrelia burgdorferi plasmid cp32-2, erpC and erpD genes, complete cds	84	147
5	14	9408	8284 gblU44914		Borrelia burgdorferi plasmid cp32-2, erpC and erpD genes, complete cds	72	568
5	15	10122	9427 gblU30617		Borrelia burgdorferi Bbk2.11 (bbk2.10), complete cds	93	560
5	16	10533	11324 gblU44912		Borrelia burgdorferi plasmid cp32-1, erpA and erpB genes, complete cds	93	790
5	17	11590	11330 gblU449131		Borrelia burgdorferi plasmid cp32-4, erpH gene, complete cds	95	261

Borrelia burgdorferi - Coding regions containing to know proteins

173	1431	552	511	801	579	1075	927	379	596	390	384	354	210	440
96	95	100	100	66	86	94	98	68	85	6	66	66	97	95
Borrelia burgdorferi plasmid cp18, OspE (ospE) gene, partial cds	Borrelia burgdorferi plasmid cp18, OspE (ospE) gene, partial cds	B.burgdorferi plasmid, orfA, B, C, D, E, & F genes, clone pOMB14 and pOMB17	B.burgdorferi plasmid, orfA, B, C, D, E, & F genes, clone pOMB14 and pOMB17	B.burgdorferi plasmid, orfA, B, C, D, E, & F genes, clone pOMB14 and pOMB17	B.burgdorferi plasmid, orfA, B, C, D, E, & F genes, clone pOMB14 and pOMB17	B.burgdorferi plasmid, orfA, B, C, D, E, & F genes, clone pOMB14 and pOMB17	Borrelia burgdorferi 2.9-5 locus, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete	Borrelia burgdorferi 2.9-2 locus, ORF-C gene, partial cds, ORF-D, REP+, REP-, and lipoprotein	Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF. A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi 2.9-6 locus, ORF-A-D genes, complete cds and REP+ gene, partial cds	Borrelia burgdorferi B31 BlyA (blyA) and BlyB (blyB) genes, complete cds	Borrelia burgdorferi 2.9-6 locus, ORF-A-D genes, complete cds and REP+ gene, partial cds	Borrelia burgdorferi B31 BlyA (blyA) and BlyB
588 gblU42599 	808 gblU425991	636 emblX87201lB BBRGABCD	185 emblX87201lB BBRGABCD	788 emblX87201IB BBRGABCD	519 emblX87201IB BBRGABCD	158 emblX872011B BBRGABCD	526 gbiU45425i	564 gblU454221	16 gblU454211	gbIU454211	21 gblU45426I	146 gblU967141	97 gbIU45426I	76 gblU967141
11588	11808	13636	14185	14788	15519	16158	18526	18564	19116	19775		20446	20797	21076
11761	13256	14187	14727	15588	16097	17276	17558	19040	19712	20164	20504	20799	21006	21903
18	19	50	21	22	23	24	25	26	27	28	29	30	31	32
5	S	2	2	S.	2	5	2	ν.	5	v	2	<u>v</u>	S	5

Borrelia burgdorferi - Coding regions containing to know proteins

	151	467	286	242	317	381	495	300	435	447	465	374	135
	94	06	93	95	96	95	06	76	66	97	96	86	87
(blyB) genes, complete cds	Borrelia burgdorferi B31 BlyA (blyA) and BlyB (blyB) genes, complete cds	Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	Borrelia burgdorferi (clone BbK3.168) phoA fusion protein gene, partial cds
17	21623 gblU967141	22051 gblU454211	22516 gblU454211	22840 gblU454211	3080 gblU454211								804 gblL314251 1
	7017	2205	2251	2284	2308(23388	23750	29417	29980	30357	30740	31215	32804
01770	714/0	81522	22806	23082	23397	23768	24331	29986	30414	30803	31204	31775	33577
33	C C	45.	35	36	37	38	39	51	25	53	45	55	59
4	7	0	χ,	S	2	2	ς	<u>ي</u>	0	0	2	2	2

Borrelia burgdorferi - Coding regions containing to know proteins

657	1590	1212	510	693	375	437	193	140	362	309	756	675	447	1155	345
100	86	100	100	66	86	77	80	96	96	100	66	100	100	100	100
Borrelia burgdorferi B31 outer surface protein C (ospC) gene, complete cds	Borrelia burgdorferi 26 kb plasmid GMP synthetase (guaA) gene. complete cds	Borrelia burgdorferi 26 kb plasmid IMP dehydrogenase (guaB) gene, partial cds	Borrelia burgdorferi 26 kb plasmid IMP dehydrogenase (guaB) gene, nartial cds	Borrelia burgdorferi transposase-like protein (tra) gene, partial cds	Borrelia burgdorferi transposase-like protein (tra) gene, partial cds	Borrelia burgdorferi 2.9-3 locus, ORF-C gene, partial cds, ORF-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi 2.9-4 locus, ORF-C gene, partial cds, ORF-D, REP+, REP-, and lipoprotein (LP) genes.	Borrelia burgdorferi 16 kb plasmid DNA fragment	Borrelia burgdorferi transposase-like protein (tra) gene, partial cds	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence
9022 gblU01894l	1425 gblL258831	2664 gblU133721	1686 gbIU13372I	3 gbIU85588I	677 gbIU85588I	5847 gblU454231	746 gbiU45424i	.087 gblU84396l	876 gblU855881	07	767 gblU43414l	862 gblU43414l	255 gblU43414I	467 gbIU43414I	735 gbIU43414I
	9836 1	11435	12195 1	695		25041 25	1420	14287 14				5188 58	7.		9079
16	17	18	61	=	7	39	7	12		-	7	<u>20</u>	4	v.	9
9	9	9	9	7	7		∞	∞ 0	× c	2	2	6	9	6	6

Borrelia burgdorferi - Coding regions containing to know proteins

	9116	603	738	273	372	278		143	290	531		713	224	1202	519	414	576		210
	9	100	100	66	66	78		16	91	66		9 <u>8</u>	88	82	81	78	84		91
Borre is hirodorferi linear alacaid la IC DMA	complete sequence	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	Borrelia burgdorferi 2.9-2 locus, ORF-C gene, partial cds, ORF-D, REP+, REP-, and linoprofein	(LP) genes, complete cds	Borrelia burgdorferi 16 kb plasmid hypothetical protein gene, complete cds	Borrelia burgdorferi Ip21 circular plasmid,	Borrelia burgdorferi exported neurotoxin-like	Protein gene, complete cds	complete sequence	Borrelia burgdorferi Ip21 circular plasmid, complete sequence	Borrelia burgdorferi plasmid cp18, OspE (ospE)	B.burgdorferi repeated DNA element, 30.5 kb circular plasmid conv	Borrelia burgdorferi Ip21 circular plasmid,	Borrelia burgdorferi Ip21 circular plasmid,	complete sequence	borrella burgdorferi 1p21 circular plasmid, complete sequence
214 ghii 1434141		2 gblU43414I	107 gblU43414I	3027 gblU434141	241 gb U43414	604 gbIU45422I		2886 gbIU 123321	842 gbIU036411	983 gblL16625l	901 ohi 1036/11	5010000411	467 gblU036411)41 gblU425991	88 emblX87127IB BPBRGEA	gblU036411	968 gblU036411		44 8010030411
921		10972	1110	1302	1324	709 I	000	7886	842	683	4901		4467	5041	7788	8355	8968	0544	1
10224	0.0	10370	11844	13299	13612	2164	7076	0807	m	1525	4008		4691	6348	6673	7786	8393	0000	2
7	C	∞	9	10	11	7	,	0		2	9			∞	6	10	11	10	-
6	C	ر ب	6	6	6	10	5	2	13	13	13	-	CI	13	13	13	13	13	

Borrelia burgdorferi - Coding regions containing to know proteins

	89 396			77 267	95 296	93 594		051 150	1 350	701		9 413		180 180	7 221					5 303		
					6	6			[6	1001	2	66			. 97		6	95	9. 9	95	<u>0</u> 0 80	95 97 97 98 99
Bornelia huradorfari mastain 202 zene	Borrelia hirodorferi profesin p23 gene, complete cus	Borrelia burgdorferi outer surface protein D (ospD)	gene, complete cds	Borrella burgdorferi (clone 8) s3 gene, complete cds	Borrelia burgdorferi plasmid cp32-1 PCR target site, nartial sequence	Borrelia burgdorferi plasmid cp32-2, erpC and	erpD genes, complete cds Rorrelia hundorferi plasmid cn22 2 cmC cnd	exposition prayment characters, exp. and exp. genes, complete cds	Borrelia burgdorferi strain 297CH putative outer	Rorrelia hitrodorferi plasmid cn32-4 emH gene	complete cds	Borrelia burgdorferi plasmid cp32-4, erpH gene,	Borrolio burndonfoni alcomid 220 / 2011	complete cds	Borrelia burgdorferi plasmid cp18, OspE (ospE)	Dome in the state of the contract of the contr	Domena purguonen 2.9-1 locus, UKF 5-8, UKF-	A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	A-D. REP+, REP-, and lipoprotein (LP) genes, complete cds Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-	A-D. REP+, REP-, and lipoprotein (LP) genes, complete cds Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	A-D. REP+, REP-, and lipoprotein (LP) genes, complete cds Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-	A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes,
621710hll 316161	6671 phl 31616	2854 gblM97452l	2 V V V V V V V V V V V V V V V V V V V	65/gblL411511	4 gbIU609631	834 gblU44914l	581 ohli 1449141	E01011010	2257 gbIU809561	ph[144913]		143 gblU449131	182 ahl 1440121	BUI CFF OIDS	360 gbiU42599I	4 phl 1454211			317 gblU454211	gbIU454211	317 gblU454211 658 gblU454211	gbIU454211
17177	1299	2854	11000	365/	4	834	1581	1001	2257	2964		5143	5183	2010	5360	4			317	317	3178	3178
5768	6126	3660	00,0	5150	849	1427	2168		2946	3794		4334	5360	7000	5581	306			664	664	664	664
7	2	S	,	n	-	2	~	,	4	5		9	1	`	8	-			2	2	3 2	3 2
141	14	16		91	21	21	21		21	21		21	21	i	21	22		•	22	22	22 22	22 22

Borrelia burgdorferi - Coding regions containing to know proteins.

	94 750	100 378	100 204	96 603	96 221	94 362	80 220	87 478	98 309	96 219	98 610	97 419	100 786
sednence	Borrelia burgdorferi putative vls recombination cassettes VIs2-VIs16b (vls) gene, complete sequence	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	B.burgdorferi repeated DNA element, 30.5 kb circular plasmid copy	B.burgdorferi repeated DNA element, 30.5 kb circular plasmid copy	Borrelia burgdorferi strain B31 2.9-like locus, OrfC, OrfD, Rev (rev), lipoprotein (LP), and 36 kDa-like orf2 genes, complete cds, and 36 kDa-like orf1 gene, partial cds	Borrelia burgdorferi 2.9-7 locus, ORF-A-D, REV, and lipoprotein (LPA and LPB) genes, complete cds	Borrelia burgdorferi 2.9-3 locus, ORF-C gene, partial cds, ORF-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi 2.9-4 locus, ORF-C gene, partial cds, ORF-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi (clone BbK2.5-6) unknown protein gene, complete cds	Borrelia burgdorferi protein p23 gene, complete cds	B.burgdorferi repeated DNA element, 30.5 kb circular plasmid copy	B.burgdorferi repeated DNA element, 30.5 kb circular plasmid conv
	108 gblU76406	760 gbIU43414I	536 gblU43414I	82 emblX87127IB BPBRGEA	882 emblX87127lB BPBRGEA	2573 gblAF000270I	2621 gblU454271	49 gbIU454231	55 gblU45424	434 gblL316151	258 gblL31616l		45 emblX87127IB BPBRGEA
	5108	092	1536	82	682	2573	2621	3149	4355	434	2258	686	1545
	4056	383	1333	684	903	2181	3073	3745	4663	997	1395	757	092
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+	74	25	25	56	56	76	26	56	50 26	/7	27	20	30

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			BPBRGEA	circular plasmid copy		
2158		2802	802 emblX87127lB BPBRGEA	B.burgdorferi repeated DNA element, 30.5 kb circular plasmid copy	100	645
3247		4230	230 gblU425991	Borrelia burgdorferi plasmid cp18, OspE (ospE) gene, partial cds	95	976
450		995	995 gbIU72996I	Borrelia burgdorferi plasmid cp32-5, erpI gene, complete cds	100	546
1008		2159	159 gbIU787641	Borrelia burgdorferi plasmid cp32-1, erpA and erpB2 genes, complete cds	100	1152
2253		2882	882 gblU44914l	Borrelia burgdorferi plasmid cp32-2, erpC and erpD genes, complete cds	86	379
3050	l l	3628	628 gblU449141	Borrelia burgdorferi plasmid cp32-2, erpC and erpD genes, complete cds	93	57.7
C)		176	176 gblU03396l	Borrelia burgdorferi B31 Ala-tRNA (alaT), Ile- tRNA (ileT), 16S rRNA, 23S rRNA (rrlA and rrlB), and 5S rRNA (rrfA and rrfB) genes, complete sequence	91	174
976		737	gblM88330l	Borrelia burgdorferi 23S ribosomal RNA gene	100	240
1		525	525 emblX87201IB BBRGABCD	B.burgdorferi plasmid, orfA, B, C, D, E, & F genes, clone pOMB14 and pOMB17	77	159
672		28	28 gbIU449141	Borrelia burgdorferi plasmid cp32-2, erpC and erpD genes, complete cds	92	571
850		653	653 gbIU42598I	Borrelia burgdorferi plasmid cp32-3, ErpG (erpG) and BapA (bapA) genes, complete cds	100	133
1516		686		B.burgdorferi ospG and bapA genes	100	534
2200		1604	91B	B.burgdorferi ospG and bapA genes	100	597
2602		3132		Borrelia burgdorferi plasmid cp32-3, ErpG (erpG) and BapA (bapA) genes, complete cds	66	529
196		999		B.burgdorferi plasmid, orfA, B, C, D, E, & G genes, clone pOMB10	76	170
1505		957	957 emblX87202IB	B.burgdorferi plasmid, orfA, B, C, D, E, & G	68	176
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burgdorferi
Borrelia

BBRGBCDE BBRGBCDE BBRGBCDE BBRGABCD BBRGABCD BBRGABCD BBRGABCD BBRGABCD BBBRGBABCD BBBRGBABCD BBBRGBABCD BBBRGBABCD BBBRGABCD BBBRGABCD BBBRGABCD BBRGABCD BBBRGBABCD BBRGABCD BBBRGBABCD BBBRGB		137	291	284	168	465	1179	1269	411	785	572	571	236	356	392
BBRGBCDE BBRGBCDE BBRGBCDE BBRGABCD BBRGABCD BBRGABCD BBRGABCD BBRGABCD BBRGABCD BBBRGBABCD BBBRGBABCD BBBRGBABCD BBBRGBABCD BBRGABCD BBBRGBABCD BBBRGABCD BBBRGABCD		91	94	91	93	100	100	66	66	08	80	65	93	96	06
BBRGBCDE BBRGBCDE BBRGBCDE BBRGABCD BBRGABCD BBRGABCD BBRGABCD BBRGABCD BBBRGBABCD BBBRGBABCD BBBRGBABCD BBBRGBABCD BBBRGABCD BBBRGABCD BBBRGABCD BBRGABCD BBBRGBABCD BBRGABCD BBBRGBABCD BBBRGB	genes, clone nOMB10	Borrelia burgdorferi plasmid cp18, OspE (ospE)	B.burgdorferi plasmid, orfA, B, C, D, E, & F genes, clone pOMB14 and pOMB17	B.burgdorferi repeated DNA element, 30.5 kb circular plasmid copy	B.burgdorferi repeated DNA element, 30.5 kb	Borrelia burgdorferi putative vls recombination assettes Vls2-Vls16b (vls) gene, complete	Sorrelia burgdorferi putative vls recombination assettes VIs2-VIs16b (vls) gene, complete equence	Sorrelia burgdorferi putative vls recombination assettes Vls2-Vls16b (vls) gene, complete equence	3.burgdorferi plasmid, orfA, B, C, D, E, & F enes. clone nOMB14 and nOMB17	S. burgdorferi plasmid, orfA, B, C, D, E, & F enes, clone pOMB14 and nOMB17	burgdorferi plasmid, orfA, B, C, D, E, & F enes, clone pOMB14 and nOMB17	orrelia burgdorferi plasmid cp18, OspE (ospE) ene, partial cds	orrelia burgdorferi transposase-like protein (tra) ene, partial cds	burgdorferi repeated DNA element, 30.5 kb rcular plasmid copy	Borrelia burgdorferi strain B31 2.9-like locus, OrfC, OrfD, Rev (rev), lipoprotein (LP), and 36 kDa-like orf2 genes, complete cds, and 36 kDa-like
9 3 2353 9 4 2574 9 5 2874 2 3028 0 1 596 1 596 1 1753 2 1753 3 1172 17 4 1745 2 2 1133 13 2 635 17	BBRGBCDE	gbIU425991	emblX872011B BBRGABCD	emblX87127IB BPBRGEA	emblX87127IB BPBRGEA	gbIU764061	gbIU764061	gbIU76406I			ED C				
E 4 2 0 1 2 E 4 2 1 2		155	2284	2572	2861	132	575	1732	411	1127	47	2338	1384	4	1741
		2353	2574	2874	3028	296	1753	3000	-	342	1172	1745	1133	360	635
3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3		8	4	S.	9	_	7	3	1	2	m .	4	7	-	2
		39	39	36	39	40	40	40	41	41	41	41	45	43	43

Borrelia burgdorferi - Coding regions containing to know proteins

	85 421	95 259	89 374	99 135	84 153	90 386	90 230	96	00 692	00 564	99 603	98 315	95 525	94 483
							5	5	100	100	6	6		6
orf oene nartial ode	Borrelia burgdorferi 2.9-3 locus, ORF-C gene, partial cds, ORF-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	Borrelia burgdorferi (clone BbK3.168) phoA fusion protein gene, partial cds	Borrelia burgdorferi plasmid cp32-1, erpA and erpB2 genes, complete cds	Borrelia burgdorferi outer surface protein E (OspE) gene, complete cds	Borrelia burgdorferi plasmid cp32-1, erpA and erpB genes, complete cds	Borrelia burgdorferi plasmid cp18, OspE (ospE) gene, partial cds	Borrelia burgdorferi plasmid cp18, OspE (ospE) gene, partial cds	Borrelia burgdorferi plasmid cp18, OspE (ospE) gene, partial cds	Borrelia burgdorferi plasmid cp18, OspE (ospE) gene, partial cds	B.burgdorferi plasmid, orfA, B, C, D, E, & F genes, clone pOMB14 and pOMB17	Borrelia burgdorferi 2.9-5 locus, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi 2.9-4 locus, ORF-C gene, partial cds, ORF-D, REP+, REP-, and lipoprotein
	1784 gbIU454231	2318 gblU454211	178 gblU60642i	1761 gblL314251	3 gbIU78764	1453 gblL139241	gblU44912l	338 gblU425991	966 gblU425991	.527 gblU42599I	2111 gblU42599I	2851 emblX872011B BBRGABCD	526 gbIU45425i	724 gblU45424I
	1784	2318	178	1761	3	1453	2893	338	996	1527	2111	2851	526	724
	2242	2860	1158	2531	287	2037	2663	174	259	964	1509	2537	7	1245
	3	4	1	(C)	 "	m I	4	1	2	<i>c</i>	4	S		2
	43	43	44	44	45	45	45	46	46	46	46	46	47	47

Borrelia burgdorferi - Coding regions containing to know proteins

651	327	91	804	909	1596	612	269	146	140	146	422	489	101
68	87	100	66	66	86	66	98	94	94	98	81	66	100
Borrelia burgdorferi 2.9-4 locus, ORF-C gene, partial cds, ORF-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi plasmid cp32-2, erpC and erpD genes, complete cds	Borrelia burgdorferi plasmid cp32-6, erpK gene, complete cds	Borrelia burgdorferi plasmid cp32-6, erpK gene, complete cds	Borrelia burgdorferi putative vls recombination cassettes VIs2-VIs16b (vls) gene, complete sequence	Borrelia burgdorferi putative vls recombination cassettes Vls2-Vls16b (vls) gene, complete sequence	Borrelia burgdorferi plasmid cp18, OspE (ospE) gene, partial cds	Borrelia burgdorferi plasmid cp32-2, erpC and erpD genes, complete cds	B.burgdorferi plasmid, orfA, B, C, D, E, & G genes, clone pOMB10	B.burgdorferi plasmid, orfA, B, C, D, E, & F genes, clone pOMB14 and pOMB17	Borrelia burgdorferi plasmid cp18, OspE (ospE) gene, partial cds	Borrelia burgdorferi plasmid cp18, OspE (ospE) gene, partial cds	Borrelia burgdorferi strain B31 2.9-like locus, OrfC, OrfD, Rev (rev), lipoprotein (LP), and 36 kDa-like orf2 genes, complete cds, and 36 kDa-like orf1 gene, partial cds	Borrelia burgdorferi strain B31 2.9-like locus, OrfC, OrfD, Rev (rev), lipoprotein (LP), and 36 kDa-like orf2 genes, complete cds, and 36 kDa-like
1321 gblU45424 	2	1182 gb U72997	1244 gbIU72997I	18 gblU76406l	704 gblU76406l	2	2487 gbIU44914I	236 emblX87202lB BBRGBCDE	6	0	1	581 gblAF0002701	719 gblAF0002701
1971	363	412	2047	713	2308	613	2203	8	179	250		93	883
3	1	7	3		2	1	33		2	3	9		2
47	48	48	48	49	49	51	51	52	52	52	52	53	53

Borrelia burgdorferi - Coding regions containing to know proteins

				orf1 gene, partial cds		
C	3 1107	8	811 gblAF000270	Borrelia burgdorferi strain B31 2.9-like locus, OrfC, OrfD, Rev (rev), lipoprotein (LP), and 36 kDa-like orf2 genes, complete cds, and 36 kDa-like orf1 gene, partial cds	100	289
4	1447	1064	064 gblAF000270I	Borrelia burgdorferi strain B31 2.9-like locus, OrfC, OrfD, Rev (rev), lipoprotein (LP), and 36 kDa-like orf2 genes, complete cds, and 36 kDa-like orf1 gene, partial cds	96	381
5	1742		380 gbiU45427I	Borrelia burgdorferi 2.9-7 locus, ORF-A-D, REV, and lipoprotein (LPA and LPB) genes, complete cds	93	362
9	1949	I	740 gblU45426I	Borrelia burgdorferi 2.9-6 locus, ORF-A-D genes, complete cds and REP+ gene, partial cds	86	210
	3		434 gblU45422l	Borrelia burgdorferi 2.9-2 locus, ORF-C gene, partial cds, ORF-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	92	326
2	1580	471	471 gblAF0002701	Borrelia burgdorferi strain B31 2.9-like locus, OrfC, OrfD, Rev (rev), lipoprotein (LP), and 36 kDa-like orf2 genes, complete cds, and 36 kDa-like orf1 gene, partial cds	86	362
3		2109	109 emblX87127IB BPBRGEA	B.burgdorferi repeated DNA element, 30.5 kb circular plasmid copy	84	246
4	1	1800	gblL314251	Borrelia burgdorferi (clone BbK3.168) phoA fusion protein gene, partial cds	06	118
J	899	111		B.burgdorferi plasmid, orfA, B, C, D, E, & F genes, clone pOMB14 and pOMB17	75	519
2		694		B.burgdorferi repeated DNA element, 30.5 kb circular plasmid copy	72	786
n	_	1410		B.burgdorferi plasmid, orfA, B, C, D, E, & F genes, clone pOMB14 and pOMB17	95	498
-	284	3		B.burgdorferi plasmid, orfA, B, C, D, E, & F genes, clone pOMB14 and pOMB17	6/	260
77	878	282	282 emb X87202IB	B.burgdorferi plasmid, orfA, B, C, D, E, & G	74	501

Borrelia burgdorferi - Coding regions containing to know proteins

	35	510	204	300	435	440	207	384	390	342	374	393	281	
	78	100	100	93	96	94	86	66	86	66	86	96	85	
genes, clone pOMB10	Borrelia burgdorferi plasmid cp18, OspE (ospE) gene, partial cds	Borrelia burgdorferi linear plasmid Ip16 DNA, complete sequence	Borrella burgdorferi linear plasmid lp16 DNA, complete sequence	Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	Borrelia burgdorferi B31 BlyA (blyA) and BlyB (blyB) genes, complete cds	Borrelia burgdorferi 2.9-6 locus, ORF-A-D genes, complete cds and REP+ gene, partial cds	Borrelia burgdorferi 2.9-3 locus, ORF-C gene, partial cds, ORF-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi strain B31 2.9-like locus, OrfC, OrfD, Rev (rev), lipoprotein (LP), and 36 kDa-like orf2 genes, complete cds, and 36 kDa-like orf1 gene, partial cds	Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	Borrelia burgdorferi 2.9-2 locus, ORF-C gene, partial cds, ORF-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	
BBRGBCDE	gblU425991	54 gblU43414l	117 gblU43414l	75 gbIU60642I	641 gblU60642	018 gbiU60642i	275 gblU96714I	600 gblU45426I	946 gblU454231	gbIAF000270I	gbIU60642I	28 gbIU60642I	12 gblU45422l	17 77 77 11 17 70 61
	910	54	1117	75	641	1018	275	009	946	1083	925	1328	12	012
+	1704	263	1320	647	1075	1530	3	217	557	1424	2	936	464	1256
	<u>r</u>		7		2	3		7	с	4	1	7		<u></u>
+	62	64	64	99	99	99	07	92	9	70	75	75	76	76

Borrelia burgdorferi - Coding regions containing to know proteins

_	90 379	97 651	80 255	99 1198	91 347	84 440	80 151	86 486	97 148	97 135	98 195	98 243	98 447
										0,	5	6	6
cds	Borrelia burgdorferi 2.9-2 locus, ORF-C gene, partial cds, ORF-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi 2.9-4 locus, ORF-C gene, partial cds, ORF-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	Borrelia burgdorferi putative vls recombination cassettes Vls2-Vls16b (vls) gene, complete sequence	Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi B31 BlyA (blyA) and BlyB (blyB) genes, complete cds	Borrelia burgdorferi B31 BlyA (blyA) and BlyB (blyB) genes, complete cds	Borrelia burgdorferi 2.9-2 locus, ORF-C gene, partial cds, ORF-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi 2.9-7 locus, ORF-A-D, REV, and lipoprotein (LPA and LPB) genes, complete cds	Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	Borrelia burgdorferi plasmid cp32-4, sequence at
	2 gblU45422I	509 gblU45424l	034 gblU43414l	202 gbIU764061	360 gblU454211	gblU967141	36 gblU967141	289 gblU454221	54 gbIU45427I	gbIU60642I	31 gbIU60642I	.23 gbIU60642I	508 gbIU60642I
	2	209	1034	1202	360	1008	636	289	954	3	131	323	\$08 8
	433	1159	657	C	-	358	791	891	1151	137	325	565	954
		2	7	_	-	7	<u>e</u>	= -	7	=	7	<i>π</i>	4
		7.1	81	83	8	85	85	98	98	8	88 88	88 80 80	× × ×

Borrelia burgdorferi - Coding regions containing to know proteins

201	313	. 331	368	243	458	472	380	234	220	234	477	886	146
86	26	86	96	76	06	94	70	100	86	100	66	66	100
Borrelia burgdorferi plasmid cp32-2, sequence at position 5kb	Borrelia burgdorferi 2.9-2 locus, ORF-C gene, partial cds, ORF-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi 2.9-5 locus, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	Borrelia burgdorferi strain B31 2.9-like locus, OrfC, OrfD, Rev (rev), lipoprotein (LP), and 36 kDa-like orf2 genes, complete cds, and 36 kDa-like orf1 gene, partial cds	Borrelia burgdorferi plasmid cp32-2, erpC and erpD genes, complete cds	Borrelia burgdorferi plasmid cp18, OspE (ospE) gene, partial cds	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	Borrelia burgdorferi linear plasmid Ip16 DNA, complete sequence	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	Borrelia burgdorferi putative vls recombination cassettes Vls2-Vls16b (vls) gene, complete sequence	Borrelia burgdorferi 2.9-6 locus, ORF-A-D genes.
891 gbIU60640I	34 gbIU454221	578gblU45421I	940 gblU454211	245 gblU454251	282 gblAF000270	3 gbIU44914I	264 gblU42599I	408 gblU43414l	757 gblU43414i	440 gblU43414l	837 gblU43414l	911 gblU76406	242 gblU45426l
168	34	578	940	245	282	3 8	264	408	757	440 g	837	91118	242 g
1091	927	162	572	m	749	206	827	175	329	207	361	3	388
3			2		7	Ţ	-		7		- 7	1	1
88	91	93	93	96	94	97	86	99	66	IOI	101	102	104

Borrelia burgdorferi - Coding regions containing to know proteins

					complete cds and REP+ gene, partial cds		
104	7	595		386 gblU967141	Borrelia burgdorferi B31 BlyA (blyA) and BlyB (blyB) genes, complete cds	100	210
107		2	81]	811 gblU454251	Borrelia burgdorferi 2.9-5 locus, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	95	789
8	-	264	4	4 gblL316161	Borrelia burgdorferi protein p23 gene, complete cds	98	201
5	7	298	173	173 gblL31616l	Borrelia burgdorferi protein p23 gene, complete cds	3 8	396
601	m	807	580	580 gblL31615l	Borrelia burgdorferi (clone BbK2.5-6) unknown protein gene, complete cds	66	228
10			456	456 gblU454211	Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	95	456
10	2	450	761	gbIU454211	Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	93	310
11	=-	787	215	215 gblU45421	Borrelia burgdorferi 2.9-1 locus, ORF 5-8, ORF-A-D, REP+, REP-, and lipoprotein (LP) genes, complete cds	68	405
61		653	84	84 gbiU60642i	Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	86	300
21	=-	719	123		Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	86	374
77 6	=	403	2	gblU44914I	Borrelia burgdorferi plasmid cp32-2, erpC and erpD genes, complete cds	85	391
87	-	175	408	408 gblU43414l	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	100	234
78	2	329	700	700 gblU43414l	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	66	356
67.		458	697	IIB D	B.burgdorferi plasmid, orfA, B, C, D, E, & F genes, clone pOMB14 and pOMB17	100	238
132	-	234	467	467 gblU43414	Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	100	234

Borrelia burgdorferi - Coding regions containing to know proteins

171	243	331	513	153	432	495	144	296	351
66	80	78	100	100	86	94	86	88	76
Borrelia burgdorferi linear plasmid lp16 DNA, complete sequence	560 emblX87127IB B.burgdorferi repeated DNA element, 30.5 kb BPBRGEA circular plasmid copy	4 emblX87202lB B.burgdorferi plasmid, orfA, B, C, D, E, & G BBRGBCDE genes, clone pOMB10	Borrelia burgdorferi B31 BlyA (blyA) and BlyB (blyB) genes, complete cds	Borrelia burgdorferi B31 BlyA (blyA) and BlyB (blyB) genes, complete cds	Borrelia burgdorferi plasmid cp32-3, ErpG (erpG) and BapA (bapA) genes, complete cds	3 emblX871271B B.burgdorferi repeated DNA element, 30.5 kb circular plasmid copy	Borrelia burgdorferi Ip21 circular plasmid, complete sequence	Borrelia burgdorferi plasmid cp32-4, sequence at position 4-6kb	Borrelia burgdorferi GrpE protein homologue gene, DnaK protein homologue gene, and DnaJ protein homologue gene, complete cds's
660 gblU43414I	emblX87127IB BPBRGEA	emblX87202lB BBRGBCDE	33 gblU967141	276 gblU967141	498 gbIU42598I	emblX87127IB BPBRGEA			2 gblM96847I
099	260	4	33	276	498	3	2	542	2
388	3	339	554	124	29	497	193	3	352
7				2	=-			=	
132	133	134	141	141	143	144	146	147	153



TABLE 6.

Borrelia burgdorferi - Putative coding regions of novel proteins not similar to know proteins

Contig ID	ORF ID	Start (nt)	Stop (nt)
2	4	2730	3554
2	5	3559	3410
2	7	5464	3869
2	13	10502	9999
2	17	13800	13576
2	19	15368	15204
2	28	21155	21400
2	50	41944	42186
2	58	53786	52911
2	59	54816	53773
2	61	57393	55813
2	63	57882	57682
2	65	60898	60203
2	66	61441	62070
2	67	62078	62692
2	70	65896	66540
2	74	70203	69910
2	78	71818	71399
2	80	72956	74032
2	81	73515	73267
2	90	92181	92525
2	91	92968	92555
2	108	109872	110057
2	112	112408	112812
2	113	112858	113037
2	114	113035	113460
2	115	113506	113724
2	119	114325	114852
3	6	3279	4079
3	8	5156	6019
3	54	42256	42789
3	59	47264	47506
3	60	47673	48692
3	63	51475	51026
3	70	60330	60575
3	71	61050	61349
3	72	61347	61670
3	74	63917	64303
3	86	75347	75532
3	88	76593	77384
3	99	89769	89005
3	102	91278	91661
3	103	92137	92463
3	105	92423	92785
3	108	93467	93886
3	115	98262	98681

Borrelia burgdorferi - Putative coding regions of novel proteins not similar to know proteins

3	121	102227	102904
3	126	111308	110055
4	6	3751	4179
4	7,	4218	5042
4	19	16115	15516
4	20	17028	16075
4	21	17379	17092
4	22	17735	17397
4	24	19243	18785
4	25	18942	19196
4	26	20677	19259
4	27	19431	19751
4	29	21376	20876
4	30	21899	21423
4	31	22918	21845
4	33	23951	23553
4	37	26253	25627
4	38	26991	26332
4	39	28181	26931
4	40	29175	28522
4	43	30605	30342
4	45	34906	33548
4	48	35750	35932
5	3	2102	1527
5	5	2656	2393
5	7	3460	2900
5	10	6544	5645
5	40	25278	24322
5	41	25235	25600
5	42	25665	25276
5	44	25881	25663
5	47	27883	27410
5	48	28351	27881
5	49	29028	28324
5	50	29454	29026
5	56	32199	31666
5 5	57	32571	32200
	58	32826	32569
5	60	32913	33245
5	61	33766	33575
5	62	34173	33742
5	64	35514	34861
6	2	954	1181
6	3	1590	1763
6	5	3400	3954
6	7	4691	5218
6	8	5187	5699

Borrelia burgdorferi - Putative coding regions of novel proteins not similar to know proteins

6	11	6498	5983
6	B	6975	6727
6		7978	7448
6	15	8479	7976
6	22	15106	15636
6	27	19999	18842
6	28	20036	20668
6	29	21814	20690
6	30	20949	21269
6	35	24136	23630
6	37	25697	26248
7	8	8100	7792
7	10	8145	8288
7	11	9374	8517
7	12	9771	9325
7	13	9652	10185
7	14	10163	9765
7	15	10517	10173
7	16	11363	10524
7	17	11904	11392
7	18	12495	11902
7	19	13516	12473
7	20	12807	13154
7	22	15149	14697
7	24	15855	15046
7	25	15503	15826
7	26	16638	15853
7	27	19344	16636
7	31	19473	19727
7	32	20067	19675
7	33	20762	20049
7	34	21136	20738
7	36	22975	23406
7	40	26667	25870
8	3	2907	4118
8	5	5898	6059
8	6	7399	8313
8	13	15645	15899
8	14	17281	16331
8	15	16905	17111
10	4	3211	3684
10	6	3857	4456
10	8	5982	5599
10	11	8038	7802
10	14	10255	10100
11	7	5688	5828
11	9	7248	7685

Borrelia burgdorferi - Putative coding regions of novel proteins not similar to know proteins

11	10	7.70	
11			8028
	13	9642	10154
12		101	370
12	2	982	680
12	3	1390	1115
12	4	1528	1388
12	5	1913	1431
12	11	7308	6616
14	2	3588	3328
14	4	4657	4815
14	9	7981	8511
15	1	1	327
15	2	325	1077
15	3	1478	657
15	4	2360	1758
15	5	2839	2507
15	9	3922	3743
15	10	4145	3900
15	11	4112	4270
15	13	7677	6127
15	14	7852	7709
15	15	8052	7825
15	16	8222	7857
16	2	1733	1936
16	3	1905	2063
16	6	5212	4220
16	7	8903	8505
17	2	1500	1709
17	5	4097	4660
17	7	6344	6189
18	1	1635	2465
18	2	2509	3306
18	3	3332	4390
18	5	4933	4727
18	7	6353	7084
18	8	7098	7625
20	7	4700	4557
22	4	2175	1228
22	5.	2132	2314
22	6	2829	2314
22	8	3254	
22	9	4408	3601
22	10	4875	4169
22	11	5343	4402
23	2		4873
23	3	2283	1537
25	6	3564	2617
23	0	3677	4147

Borrelia burgdorferi - Putative coding regions of novel proteins not similar to know proteins

26		4251	3889
28		732	1739
29		310	885
31	1	28	195
32		935	1603
32	4	1637	2332
37	2	1379	1059
42	4	2708	2388
44	2	1734	1159
44	4	2942	2532
47	4	2336	2115
50	1	908	120
52	4	674	501
56	1	152	1465
56	2	611	459
56	3	1479	2150
58	3	1691	1329
58	5	1867	2046
59	2	2018	1044
61	1	1	657
61	3	1389	1907
62	4	1115	1345
63	1	663	325
63	2	769	446
63	3	1759	1013
65	1	472	903
65	2	901	1236
67	1	387	4
67 67	2	979	401
	3	1482	961
68 69	2	451	612
	3	840	574
71	1	363	4
72 73		586	933
73	1	300	4
73	2 3	824	279
79	1	1396	1145
82		22	1119
82	1 2	701	303
84		1188	775
84	1	331	134
87	2	983 277	348
87	2	1136	2
96	1	434	267 57
96	2	748	57 557
97	2		557 650
3/		976	659

Borrelia burgdorferi - Putative coding regions of novel proteins not similar to know proteins

100			
103	1	301	2
103	2	886	299
105	1	36	509
106	1	425	3
106	3	761	600
112	1	416	799
113	1	685	59
118	1	1	489
118	2	487	753
120	2	299	691
124	1	1	630
127	1	702	322
135	1	287	3
135	2	649	407
136	1	1	645
140	2	619	332
145	1	1	480

(1) GENERAL INFORMATION:

- (i) APPLICANT: Human Genome Sciences, Inc. et al.
- (ii) TITLE OF INVENTION: Borrelia burgdorferi Polynucleotides and Sequences
- (iii) NUMBER OF SEQUENCES: 155
- (iv) CORRESPONDENCE ADDRESS:
 - (A) ADDRESSEE: Human Genome Sciences, Inc.
 - (B) STREET: 9410 Key West Avenue
 - (C) CITY: Rockville
 - (D) STATE: Maryland
 - (E) COUNTRY: USA
 - (F) ZIP: 20850

(v) COMPUTER READABLE FORM:

- (A) MEDIUM TYPE: Diskette, 3.50 inch, 1.4Mb storage
- (B) COMPUTER: HP Vectra 486/33
- (C) OPERATING SYSTEM: MSDOS version 6.2
- (D) SOFTWARE: ASCII Text
- (vi) CURRENT APPLICATION DATA:
 - (A) APPLICATION NUMBER:
 - (B) FILING DATE: Herewith
 - (C) CLASSIFICATION:
- (vii) PRIOR APPLICATION DATA:
 - (A) APPLICATION NUMBER:
 - (B) FILING DATE:
- (viii) ATTORNEY/AGENT INFORMATION:

- (A) NAME: Brookes, A. Anders
- (B) REGISTRATION NUMBER: 36,373
- (C) REFERENCE/DOCKET NUMBER: PB370PCT

(vi) TELECOMMUNICATION INFORMATION:

- (A) TELEPHONE: (301) 309-8504
- (B) TELEFAX: (301) 309-8512

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 910715 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

ATATAATTT	TAATTAGTAT	AGAATATGTT	AAACTTTACC	CTTGAATTTT	TCTACTCTAT	60
TTGTATATTC	TATAGAAAAA	ACGATTAGAA	TTAAACAAAG	CCATAACTGA	ACCAACGGTA	120
ATTAGTAGAT	AAAGGGATCA	AAATATTTTT	TATTGCAGCA	AGAATACCTT	GGTATATTAG	180
AAAAACCAAA	AGTCATAGTC	AAATCATCTT	TTGATAACAA	TCCCCAAATC	TATAATTTAT	240
TATGAAATTA	ATTGCTCCCT	TGAAAAGATT	AGTTTTTAAA	ACTACAAGAC	TACTATCAAT	300
CACTATCAGA	TAGATTAAAA	CAACCTTTAC	AAGAAAAAA	TCTTACTACT	ATTTTATTGT	360
AAATGTATTA	TAAAATAAGT	TCATGCAAAA	ACTTACAATT	TTTCACAACA	AACTACAATA	420
AAATCATGTA	AACAAACAAT	TTCTTTGAAA	ATTAAGCAAA	ТТТАТАААТА	TAAATTATAA	480
AGATATATAT	TTTTATATGA	ТСААТААТАА	AAATTAATAG	GATACTTATT	TGGAAAAATT	540
ATTGAAAAAA	CAATAAGCAT	GAATTGCCAC	AATAAGCTAA	TTGTCACTTA	ATAATTCTTG	600
TTTACTAGAC	CACATTAGTA	TAAACTCAAA	TATTGGCTAC	TATAATATAG	GGGCTTTATA	660
CGCCACATGT	TTAATGATAA	CATAAGAAAA	TATTGCAATA	ATAAAAAGAT	TGAAATATCT	720
TTATTAGAAA	AGAATCTCGA	TAATTTAGAA	AACAGAATAA	AAATCATAAC	ТААТААТАТ	780
AACGTTGAAA	ААААТАТАТТ	САААСТТТАА	СТАТАСААТТ	AATTACACCT	TAAAAATGCG	840
ТТАСАТАААА	ATTAAGGACT	АСТАТАААТА	GAAAACACCA	CATAACCTAC	AGACTCTAAA	900
GGAATAATTA	AATCCTCATA	TTTCAGTTCT	CCAAAAGTTT	AAATAGGGGC	CTTTTACTTT	960

TCTTGATTAG CATATACAT	TT ATTAAAGGC	A TCTTCTTGG(CACTATCCTA	AACTTTTTA	1020
CATTATTATT ATTTTATTO	T TTATTATTAC	C AAGATAATTO	AAGAATCTAG	ATTACAAGAT	1080
ATCAATCCTG CCATTAGT					1140
ATTTTTTCA TTTTTGAAA					1200
TCAACTTGAG AATCCGATG					1260
TTCTTAATAT ATCTAGTAA					1320
GTAATATTAA TTTTATTTA					1380
ACTTTAAATC CTGTATAGC					1440
ААААТААААТ СТТСТААТТ					1500
TTTTTTAAAT TTTCGGTTT					1560
ATGTCACTTT TCTTGCTGT					
ААААТАТТТТ ТААТААТАТ					1620
ТТАССТТТАА АААААТСАА					1680
GCTGAAAATT TGTCTGTATA					1740
AAAGAATTTC TAGAAAACT					1800
TTAACAACCA TAAAAGGCT					1860
CTATATTCTA TGCCATCTG					1920
					1980
TATTTCAAAAT AAGGTTTTAA					2040
TATTTGGCCT CTATTAAAA			TTGTTGGATA		2100
TCAACCCTTT TTAGTCCATC					2160
ATATCAGTAT GATCATAGCC					2220
TGTGCTTCAT TTTCAATAAC					2280
GAATTTTCAA AATTTATATC					2340
ТАААААТТАА ТААТТСТААА					2400
GATACCTTAA TTCTTTTTC					
TTATTTTTC CTTACCTTAT					
TCCTTTTATT AAAGACAAAA					
CTAAGCAAAG TAATAAAGTC	TTCTTTGGTT	AATGAATAAA	AGACTAGCTA	ТААТАААТТ	2640
ATTTTATTTT TCTTTACTAA	ATTCAAAATG	СТСТАААТАА	AGCAAATTAG .	AGAAATTCAA	2700

			159			
					ATAATGAACT	2760
AGCCAAAATT	TCTTCTTTG(G GTTGAGGCA	T TGGACATTG	A CAAAGAAAT(ATTTTACAAT	2820
GTCGGTATTT	TAAAACAAA	CTTCTAATC.	А ТААААТСАА	A TACAGTGCAT	TGAAAATAGA	2880
ТАТААТАААС	AATTTTTTA	AAAAAGATA	r tggtatttt	C TCACAATTCA	A TATCTATTTT	2940
ATAGAAACAC	AATAATAAT	TTTAGGAGA	T AAAGTGCTAA	A TCATGGTTCT	TTCATTTGTA	3000
TTGCTTGCAA	TTCTTCTATA	AAATATTCT	TCATTTGGGT	T ACTGATCATC	TTTAGTTAAG	3060
ATTTTTTCTA	AATCTTCTTT	ATATCCTATO	CATAAAAGCT	TATAACCTTC	TTTTACATAA	3120
TCATAAGTAA	AAAATCTTAA	ATTAAATTG/	A TAGATATTAG	CCCCAGAATA	AAGAAATATA	3180
AAGTTTTCAT	TATTATATTC	CTTTAATAA	A GATTTGCGAT	TCTTTATACT	TGGATCTGGC	3240
CCTTTTTTAA	AATTAATATC	TTCTTTACT	AGAATACTAA	ATGAACTAAA	TATTTTGTTT	3300
AATTTGGCCC	ATGTTTAATT	CAATTCCTTT	ATAAGGATTT	TCTTTGCAGT	CTTTTAAGTC	3360
TCTAGTTATT	CCTTAATAAT	ATTATCACTA	CTTTGAATAA	CAAATTTTGC	ТТТААААТТТ	3420
AATGTAAAAG	ТТТАТТАСТА	CGAGGAAATA	TCGCAAATTT	AAAACTTGAA	TGCATATCTT	3480
AAAACCTTTT	TTTGTTTTCA	AACTGATAAA	TAAGTTAAGT	ТТАТААТТАС	TAAATATATG	3540
CTTTCTTAGC	AAGCTAAGAC	САААТАТСАС	AATAGAAGTA	АТТСТСААТА	AACAAAATAC	3600
AAAAAGTAGT	TATCATATCG	TCTTTAACCT	TAAATAAGGT	TGCTATAAAC	AACCAAGATA	3660
TTTAATTTCT	TTTAAAACCC	TTATTCAATC	TTTTTAAGCA	TAGGATCTTA	TAATTATAAG	3720
AATATAATTT	TATTTACATC	TCTATATTAA	TAGAAAGATG	CAAATATGTG	ATCAAATTGT	3780
TATTTTTGTA	ATATGGAATA	GTCCTTTATA	GGGACGCTTA	ATGCTCTATA	CTTAAGATTG	3840
GAATTCTCTA	TGAAAATATA	TACTCGCTAC	CCATGTAAAG	CTGACTTATT	TTAGCACGTA	3900
TCGCTTAAAC	AATTATATTT	ATATTATCTT	TTATAAAGTT	AATTTTTTCT	TGTAGATTAT	3960
TTTTTAATAA	AAAAGGCACA	AATTACCACA	ACAAGTTCCA	GTATAAATTA	ATAGTTCTTA	4020
TCTCAACACT	AAAGTACATA	AACATCAAAT	АТСАААААТА	TATAAGAACA	ACATACTACA	4080
TTGTTTTAAT	GAAAACCTTA	AAAGGAATGG	ТТАААСТСТС	ATTAAGCTAA	AACCAATGCA	4140
AAAATATCTT	TATAAATTAG	CAAAAGAACT	AAAAGTCACA	AACAACTACC	АТАААААТТТ	4200
GGTAGTAAAT '	TCTGGAACTG	АААТТТАСТА	ТАААСТСААТ	ТАТТСТАААА	AAAATATTGC	4260
СТТАААТТАА	AGAATGCCTT	АААААААСАА	AATGCTCTGA	ТТТАААССТА	ТАСССААААТ	4320
ACAAATTTAC	TAAAGAAGAA	GATATAGATT	TAGAGAAGAT	СТТААТААТА	AAAATATTAA	4380
TATAAAAGTT (GCTCAGTATG	CTAAAGGCAA	AGAGTTTAAG	TCAAGTTTAG	АААТТАСААА	4440
GAGTAAAACT A	ATAAACTTCC	TTTAAGAATG	TTATTTAAAA	ТТТАТАСТТА	CTTGGCTTAA	4500

					TTTTGCTATA	4560
CAAAAATCTT	r acacatetaa	ATACTTTTTA	AAAAAATTTG	ATTAGTGTTA	GAATATATTC	4620
TATATTTATA	A AACTTTATT?	GCACTCATAA	ТТТТАСТААА	ТТААТАТАТТ	ATATTTAATT	4680
TATTTTTAA	A ATTTATCTCC	ATTTACCAAA	AAAACTAAAA	TAAAACTCTC	САААСТТАТА	4740
AATAAAAAA	TAAGGCAAAA	CCCCAACAAA	CTCAAGATCT	АТААТАСААА	ААТАСААТАТ	4800
AAGAATCCCA	AGCTTAAAAA	CAACCCCCTA	AAATCTTTTT	TTATTGGCGT	ТТТТАААТАА	4860
TGGTAATAAA	GAATTCCAAT	CAACACGATC	CCCCCTACAA	СТТТТСАААС	CCTATAGCTT	4920
GGCTTTTTAT	' ATTATTTTA	AATTTACATG	TCACAACAAT	AGATAATGCA	TAAAATAAGT	4980
АТТААТААА	CAAATACATT	TATAGAACCT	ATACAATTAT	TGAGCATATG	GCTAGTACTA	5040
AAAATGAAAA	TGTACAAGAT	AATATGCTAT	ТААТААААТ	TAATGGCTAC	TAAAACTTTT	5100
GAATCCACAT	TTTTTCTTTA	AAAAAATTCT	AAATTATTAA	AATAAATAGA	AATTAAAATT	5160
АССАААААТА	TTATTATAGT	AATAAATATG	TAAAGCTATT	ТТТАТТАААА	CTGATAATAA	5220
АААТАТААТА	GCTAAAATAA	САТАААТТАА	СТТТАААТТА	TATCAAAGAC	TTAGATTTAA	5280
AATATTTAAT	AAAAGGCAAA	GCTATAAACA	CCATATACTT	ATTTTATTAT	TTTTTTCATT	5340
ТТАТТТАААТ	ТААТТТАААТ	AAGACTCAAT	САААТААТСА	ATCAAACATA	TTGGGTGAAG	5400
AAAAAATAGG	GTATTCTTGG	TGAATCGTTT	TAAAAGGGGG	TATAGTAAGC	ТААААААСТС	5460
TTATTAAAGA	GGATGTTTAT	AGACTTAAAA	GTCTAATTCA	ATATGAAAGA	GGCTTTTTAA	5520
AGCTAAAAAT	GTTAAAGAAA	ATCAAATTAA	GCAACAAGAT	GGTTTTGTTT	CTATAAATAG	5580
TTTTAAAGAA	ТАТАТАСАТТ	TGCACATACC	CTTCATTATA	ACATCTACTA	ATTACACAAT	5640
ААААТАААА	ATGATTTATT	AAGAATTATT	AGTAACTTAT	AAAAACTTTA	TAAGTTACAT	5700
AGTCAAAAAT	TTAAAAATT	ААААСААААА	ATTAACGATA	TGGAAAAATT	GTATTTTATA	5760
GAAATAGAAA	TATATTTGCA	TTAAACAACT	ATGAATTTAT	AAAGATTCTA	GTAGGAGAGA	5820
AAATATGAAA	АААААААТТ	TATCAATTTA	CATGATAATG	CTAATAAGTT	TATTATCATG	5880
TAATACAAGT	GACCCCAATG	AATTAACTCG	TAAAAAAATG	CAAGACAAGA	ACGTGAAAAT	5940
TTTAGGATTT	TTAGAGAAAA	TTCAAGCAGA	TAATAAAGAA	ATTGTTGAAA	AACATATAGA	6000
AAAAAAAGAA	AAACAAATGG	TGCAGGCTGC	TTCTGTAGCA	CCTATTAATG	TAGAGAGTAA	6060
TTTCCCATAT	TATCTTCAAG	AAGAAATAGA	GATAAAAGAA	GAAGAGTTGG	TTCCAAATAC	6120
TGATGAAGAA	AAGAAGGCAG	AGAAGGCAAT	TAGCGATGGG	AGTCTTGAAT	ТТССТАААТТ	6180
AGTTGATGAT	GAAAATAAAC	TTAAAAATGA	ATCTGCGCAA	TTAGAATCTA (GTTTTAATAA	6240

			161			
TGTTTATAA	A GAAATCTTAG	G AACTTGCAGA	TTTAATACAA	GCAGAGGTGC	ATGTTGCAGG	6300
AAGGATAAA	r agctatata	A AAAAAAGAAA	A GACCACTAAA	GAAAAAGAAT	ATAAGAAGAG	6360
AGAAATTAA	G AATAAGATA	S AAAAACAGGC	TCTAATTAAG	TTGTTCAATC	AGTTATTAGA	6420
AAAAAGAGGG	GATATTGAAA	ATCTTCATAC	TCAATTAAAT	AGTGGACTTA	GCGAGAGAGC	6480
ATCTGCAAA	A TACTTTTTC	G AGAAAGCCAA	AGAAACTTTA	AAAGCTGCTA	TTACTGAAAG	6540
ATTAAATAAC	CAAACGTAAAA	ATCGGCCATG	GTGGGCAAGA	AGAACACATA	GTAATTTAGC	6600
AATACAGGCA	AAAAATGAGG	CAGAGGATGC	TTTAAACCAA	TTAAGTACTT	CTTCTTTTAG	6660
GATACTTGA	GCAATGAAAA	TAAAGGAAGA	TGTAAAACAG	CTTCTTGAAG	AAGTAAAATC	6720
TTTTCTAGAT	TCTTCAAAGA	GCAAAATCTT	TTCTAGTGGC	GATAGATTAT	ATGATTTTTT	6780
AGAGACGAGT	AAAAAAAAA	АТАТАТТТА	AAGGCTAATA	ACTTAAAATC	AAAGTCTTCT	6840
GTTAAAGGAA	GACTTTTTTA	ТААТТТТАТТ	TAAATAACGA	AAAGCTTGAT	AGTTAAAAAA	6900
TCTTTTTAT	' ТАААААТАТС	TTTACTAAAC	AGAGCTCAAA	AATGACTATA	TTTAGTATCT	6960
CTATAAAAGA	ATTTTTCAAT	ATTTTAAAAA	ATTTATAGAT	АААСАТААТС	TAAAACCATG	7020
САТТААТАСА	AACCTAAAAC	ATACTTGGTC	ACTTGTAAAA	GTAAATTGTA	TCTAACTTTT	7080
ТТТАТТТАТТ	GAATATACGT	AAAAATTCTT	TATAATTTCT	ATTTTAAAAC	GCTGCTATTT	7140
AGCAATACAA	TAAAAGGCAT	TACAGATTGC	AATCAAACAA	ACTAAAGTTT	АААТАААТА	7200
TTACCCTCTG	TTCTAATCCT	ATCAAACAAG	GTAATAAATT	СТТТАААТТТ	CTAAAAGCCT	7260
AAACTTTAAA	AGAACTTGTC	GAAAATAATA	TTTCTCTTAA	AAAAGGTTCT	AATCTTTTAT	7320
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ATAAATCAAG	CCTTCTACTT	TTTTTAAGAA	TATTTCTATT	TTTTATAAAC	TAGTTTTCTA	7440
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AAAATAGAGA	TAAAAAACTC	AATCATAAAT	AATGGTAAAA	CAAACTTAAA	CCACGTACCA	7560
TAACTCAATC	TGGATATCCC	CAATACAGCC	ATTATAACTC	CGCTGGTAGG	TGTTATCAAA	7620
TTAATAAGCC	CAGATGCAGT	CTGCATGGCA	ATAACAACTG	AAGCTCTTGG	AATTGACAAA	7680
AAATCGGCAA	GAGGAGCCAT	TATTGGCATA	GTGAGACTAG	CATGTCCTGA	TGAAGATGGA	7740
ACAACAAATC	CTATAAATAT	TTGAATAATT	TCATTCAATA	TGATAAAAAG	GGGTCTTGGA	7800
AGATTGTATA	AAAAATTAGT	AGCAGCATTT	AACATAGTAT	CTGTAATCAA	CCCATCATCA	7860
CATACTATCA	TAACACCTCT	AGCAAGTCCA	ATAACAAGAG	CAGCGGTTAG	CAGACTTTCA	7920
GAACCTTTCA	CAAACGCATC	CCACATTTCA	GTTTCACCTA	ATTTACAAAT	AAAAGCCGAT	7980
ATAATAGCAA	CTCCAAGATA	CAACATTGTC	ATTTCTTGCA	TCCACCAACC .	AAGATTAACA	8040



			163			
					CTTTTTTAAA	9840
					AAGATTTAAA	9900
	•				ТТТТТААААА	9960
CTCATTTAAC	TCATGCTTAA	ACATGCTTA	ATAAATTAAA A	TCCTCTCTTA	CTAAAGACAT	10020
AGACATGCAT	CTTGGCCCAC	CACGACCCC	TGAAAGCTCG	G CTAGACGGAA	TTCTGTGAAC	10080
TTTAATACCA	TTTTCTTCAA	ACAGCTTATT	AGTTACATGA	TTTCTAGAAT	AAGCAATTAC	10140
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TATTAAATCT (CCACCCGCAC	ATTTTATTAT	GTCAATTTTT	CTGCCTAAAT	AAAAGCTCAA	10260
AACATCTTTA A	AGCTTGGCTT	TTTCTTTTTT	' AATATTAATT	' TTATTAGAAT	TTGAATTGTA	10320
AGTTAAAACA 1	PAAATTGAGA	AATACATATO	ATCACTTGTA	AAACTTGTAA	AAACGCTATA	10380
ATCAATTTGG (GTAAAAACTG	TGTCTAAGTG	CATATAGGCT	СТСТТТТТТС	GAATTTTAAA	10440
AGCCAAAATT (GTGCTAAATG	GAGCCTTATT	TTTAAAAAGA	CTAGCAGCTA	GTTTTTCTAC	10500
AGACCCCGCT 1	PCTGTTCTTT	CTGAGATTCC	AATAACCAAA	AGATCTTTAT	ТТААААСААА	10560
CTCATCCCCA (CCTTCCAAAG	AAGTTTCTTC	CCATCTATTA	AACCAAATTG	GAACATTTTC	10620
TTTGTAAGCG (SAATGATATT	ТАААААТАТА	CTCTGCAAAT	ATTGTCTCTC	TACGTCTAAC	10680
CTTGGTATAC A	ATTTATTTTA	TTGTAATTCC	ATTGCCAATA	CTGGCAAAAG	GATCTCTGGT	10740
АААТААААСА Т	TGGGCATAG	GATCAATAAC	AAAAAGACTT	GAACCATTAA	CCCAATCATC	10800
AAGCGAAAAT I	CACAATCTT	TAAGCTCTTC	TCTTGCAACG	CCGGAAATCA	TTTTAGAAAC	10860
CATATTATCA A	CGGTTAAAT	TAGAAAAATA	ATCTTTTAAA	ATATTAATTA	CACCATCTGT	10920
TTTTATTTCT G	CTTCCAGAA	TAAATTGAGA	TATAAATTTA	TTTTTGAGCG	CTACAGAAGA	10980
AGCAAGAACT T	CACTAACAA	GATCCTCAAC	ATACTCAATT	TCAACTGAAT	TATCTTTTAA	11040
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ТАААААТТТ Т	TCATAATCA	AGGGTGTCAA	ATTTTCTAAT	TCTTCTCCTG	GCCTATGAAG	11160
CAAAACTTTT T	TCAAACGAC (CTATTTCCGA	AAATATATTT	ATTGGATTTA	AATATTCTTC	11220
TTCCATCGAT T	TCCCCCTTT A	ATGAAAATTG	TCATATATTA	AAATACTATA	GTTTATATTA	11280
AAAAACATCA A	CTATTTTTA A	ATAATATTAA	АААТАТААТА	AAATATAAAT	AAATTGAAAA	11340
AATAAAAGTT C	ТААААААСТ :	TCAAATCAAA	ААСАТАААСА	AAAAATTATG	СТААААТАСТ	11400
AATCATGAAG A	ATATTAATA (SATTAATATT	АТТААТАТТА	ACTACACACA	СТТТАТТАТТ	11460
CTCTTGTGCC T	TAATTGCAG A	ATAATAAGTC	АААААТТТА	AGCACATCAG .	АААТСАТАТТ	11520
AACACAAAAA A	CACTACTAG A	AAAGCTCTTT	ТАААААТАА	CCTTCTAATG '	TAGAATATCG	11580



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GAATATGGAA ATTATTATG					13380
CTTGCCCTAT ATACAGCTC	T CAAAATAGC	A TTAAAAGAA	AAATAATAA	CATATTTGGG	13440
GACAGTAAAT TAATAATTG	A CTATTGGTC	A AAAGGAATCT	T ATAATAGCAA	AAAATTAACA	13500
САААТТАСТА ТТААТТТАА	T CAAAAAGAC	A ACTGAACTAA	GGAAAAAATT	TGAAGAACAA	13560
GGTGGAAAAA TTTCTTTTA	T TCCAGGAAA	r gaaaatatto	G CAGATCTTGG	TTTTCATAAA	13620
ACTAAGTAGA AATATTGTC	A AAAAATACA	Г АААААСААТА	TTTCTGATTT	CAATGGTTTA	13680
TTTTTATTGT TGTACGACA	Α ΤΑΑΑΑΤΑΑ	A CCATGATTAT	GAAACTGATT	TTAAAGTTCT	13740
AGAATCTCCC TCTAAATAC	A TCAATATAGA	A TGTAATTAAA	GCTACAAATG	AATATATTTA	13800
TATTCAAATT ACAAACAAT	A GCTTAGACG1	T AGTAAAATA	AATTGGCAAA	ACACTAGTCT	13860
TAACAACGAT AAGATCGTC	r taaaaaaaga	AGATCTTACA	ATAAACAATG	AAACAGGGTA	13920
TAAAAATAAA TACAGAGAG	r tttttattgg	G ТССТААААСТ	TCATTTAAAT	TTAAAGTATA	13980
TCCACTAAAA ATTCATTCT	A AAAACAAAAA	TAGCAATAAC	TTAAGCTCAA	СТАТТАААТА	14040
TCCGTCTATT TTTAAGCTCA	ACATAACAAA	AGTAGGAATT	GAAGCAAAAA	АААСААТААА	14100
TGTTTTAATA ACAAGAACTA	А САААААТТАА	ТАТТАСТААТ	АААТСААААТ	САТТАТТАТТ	14160
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CCCCCAAGGT AAAAGAAAGC	TTATTGTCAA	AAAAAGTTAA	AACGTACAAT	TCCTTTTTGT	14700
AACTAGAATC TAAAGAATAT	GGAACAAGTT	TGGTTGTAGT	ACCAATCTTG	GAAAAATCTC	14760
CTTTTAAAGG ATCATAATTA	TATTCAAAGT	CGTCTTTCAT	AGCAAACAAA	AATTGAAAAT	14820
САААААСАТТ ААССТТАААА	GAAAGTTCAG	AAACTCTATT	TATCAAAGGA	TCATAGGCGA	14880
СТААААААСТ АААТТТАААА	ТААТССАААТ	ATCTCGGCTC	AATTTTATAA '	TACAAAGCAG	14940
GAGACATTTC TAAATTTTTA	TAAGGCGATG	ATGGTTTTTG	AGGCTCCAAA (GGACTTTGAA	15000
CAGCAGAAAT TCCAGAGTTT					15060
CAATCCCAGC TTCTTGTAGC	AAATAAGGAA	AATCTAAAGA	AAGTTTAAGC	rcagaagaag	15120

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TACTACTATT CTTATTAACC AAAGATTTTA CATCAGAATC ATATTTTTTA TTAAATGAAT	15300
ATAAAGTAGC CTTATTTTCA AACTTTAAAG TACTTCTAGA AAATAAAGGA TATCTAATAA	15360
AAGGAAGCAA GTTTAAATTT ATTTGGTTAA TAATAGAGTG CTCACTTTTT TTATCTTTAT	15420
CTTCAACTTT AAAATCTTTA TTTAAAGGAC TATACTCAAT AGTATTAAGA TATAATAAAT	15480
TTTCAAAAGT AATTAAACGA TTGTAAAAAT CAGCATGAAT TTTTATATCC GTTTTATTTT	15540
TTATATCAAA TAAATAATTT TTTATTTCAT AATTAAAGTC CTTTGGACTT GTTATGCCAT	15600
AATTATCAAA AAAAACATTA TTTCTTAAAT AAGGATTAAT GCCAAACCTA ATAAAAAAAG	15660
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TTAATTCTGT TGTTTTTTA GTATTTTTCT CCTTCACACT CTTTTTATCA TTATCTTTAT	15780
CTTCTAGATT TTTAATTTCT GGGCGCATTA TCATTTCTTT AGTATCAGCT GGAAATGTCC	15840
ATTGGTTATT GTAAAGATCT TTTTGAAAAT TCAAATCAAT ATATGGAGCA TAAATTCTCT	15900
CCAAATAAAA CCATTTTCTT GTAGGATCAT TAACATCTTT TGGTTTCTCT AAAGGAGATT	15960
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TCCTGGTAAA ACCCAATCCA AAATTTCCTT CCAAAGTTTT AAAATGCCCC AAAGTATTGC	16440
CCAAATTAAA ATCAATTCCA GAATAAAATC CCAGATTAGC ATAAATGTCA AAAATAAGCT	16500
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CATTTCTTAT ATAAGGTTTT TTACCCGAAT TATAAACAGA ATTGAAATCA AAATCCAAAA	16620
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AACCTTTTCG TGGATTTAGA CCTAAAGATG GATTAAAAAA CAAACTATCT CCCGGTCTGA	16740
AAAAAAAAGG AATATAAAAT ACTGGAACTC TTCCCATGTA AAATATGGCA TTTAAAAACC	16800
CAAAATCTCC CGAGGGCAAT GCCCATATTT TAGAAGCCTT GATTGAATAG TAAGGCTCTG	16860

			167			
GAATTTTAC	T AGTTGTTGC	A AAAGCTTGTT	CCAAAATGGT	AACATCATTO	TCTATCTTTT	16920
TTAAAACCT	T TCCTCCAAA	C GAAAGAATAT	GATCTATTTC	ATTTTTTGC	CATTTTTTTTT	16980
GAAGAATAC	C ATTTTTTAAT	TTTTAAAAAA T	GAGAATCAAA	ATCGACAAGA	AATTCATTGC	17040
САТАДАДАТ	A AAGCTTTTC	A TTGGTATCCA	TATCAAGAAT	' ATATTCAACA	TTTCCAATAG	17100
CATAAAGTT	T TTTAGAGTTC	TTATTAAGGA	CTATTCTGTC	GCCТТТААТА	TTGTGCTTTT	17160
TATTTTCTT	r aatatette	ACCAAGATAT	TAACTCTTCC	ТТСАААААТА	ATACTTTCAT	17220
CTTTAGTAAC	G TCCATAAGTG	AAATTTTCAA	GATTATCTGC	AGTTTCAATG	АТТАТТТТАТ	17280
ATCTACCAG	A TCCGGCAAGT	CCCTTTCCTT	TGATAAAAG	CTCAGGATCT	ATTCCAAACT	17340
TTTTTAAAAC	G CAATTCTCGT	' ATTTTTGAAA	CATCTGTTTC	TTTTAAACCC	TCTTTTAAGG	17400
CCCATTTTT	TAAATCCTCA	TCGGTTGAAA	GCTCAAGTTC	ТСТТАААТАА	GATTTTTGAC	17460
TTAAAGTTAG	CTTATCCCTT	TTTTTAGAAT	TTTCATCATC	TATAGTCTGG	GCAAAAATTG	17520
CATTAGAAAA	TGTTAAAAAA	АТТАААААТА	CTATAAAAGA	TTTTTTAAAA	ACATTCCTGT	17580
ATAGGAATTC	TCGCATTTTG	CAACCTCTTC	AGGAATACCA	GAAACAACGA	TATTTCCCCC	17640
TGCCAACCCA	CCATCAGGAC	CCAAATCTAT	ТАТАТААТСТ	GCCTGTTTAA	ТТАСАТССАА	17700
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TGATAAAGTT	GTTGCAGATT	GTCCTAATTT	AATATATTCA	AGTCCAACTT	СААТТАААА	17940
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AATTTCTGTA	AAAAATCCAA	CATAAGTTGC	TGGGTTTGAT	CTTGAAGTTC	TCCCTATTGG	18300
TTTTTGATTT	ATTTGAATAA	TTTTATCGAT	ТТТТСАТАС	ССААСААТАТ	CTTTAAAGCC	18360
ATCACAATAC	TTTTCATTAA	GCTTTAATCT	ACTATCAAGA	GCTGGATATA	ACACCTCGTT	18420
AAGTAAAGTA	CTTTTTCCGC	TACCAGAAAC	ACCTGTTATT	ACGGTAAAAA	CTCCCAAAGG	18480
GATACTTAAG	TCTATATTTT	TAAGATTATT	TTTATTAGAG	CCCAAAAGCA .	AAATTTCTCC	18540
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ACCAGTTAAA	CTATTTTTGC	TAAAATTAA	ATCAATCAAG (GCTCCCTTTG (CAACTATTTC	18660

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GCCAGAGCCA CTCTTGCCAG ATATTACAAC TAAACCATCT TTTGGAATAT CTACATCAAC	20340
ATTTTTTAAA TTATGTTCTT TTGCTCCTCT GACAATAATT TTTTTTTTCA AACTTTTTTC	20400

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CAAAAATTA	C ACCTCTCTT	TTTTATTAC(G AGCTATACTA	ATTTTGCTAC	TAAGCTCTTT	20460
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AGTAGTAGA	Г СТТАААААТС	CCACCTTATO	AGCATCTAAT	ATTGCAACAA	GAGATACTTC	20880
TGGAATATCT	AAGCCCTCTC	TAAGCAGGTT	' AATCCCAACA	ATAACATCGA	TTTCAGATTT	20940
TCTAAGCAAC	GAAATAACTT	CCACTCTCTC	AAGGGTATCA	AGCTCTGAAT	GTAAATATTT	21000
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			177			
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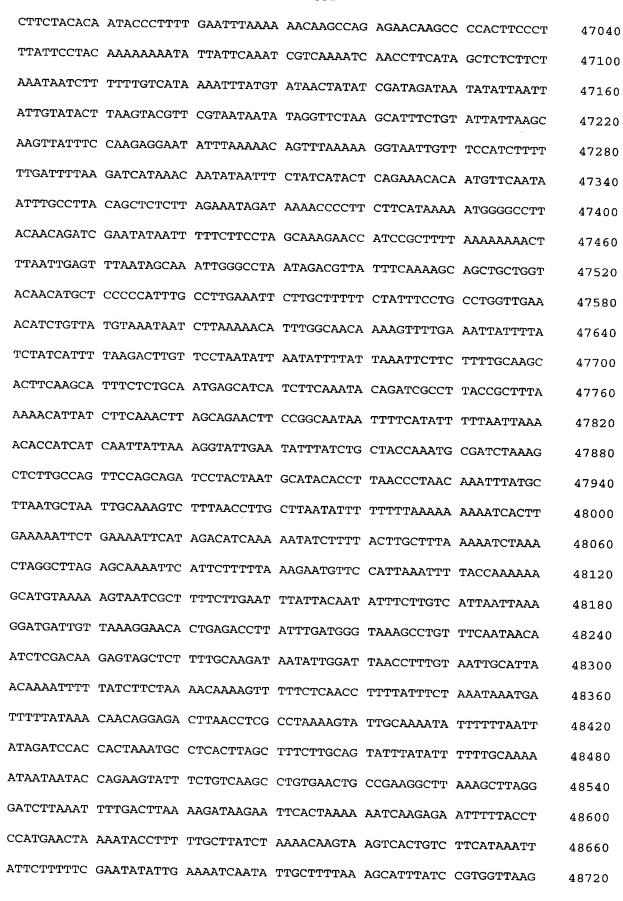
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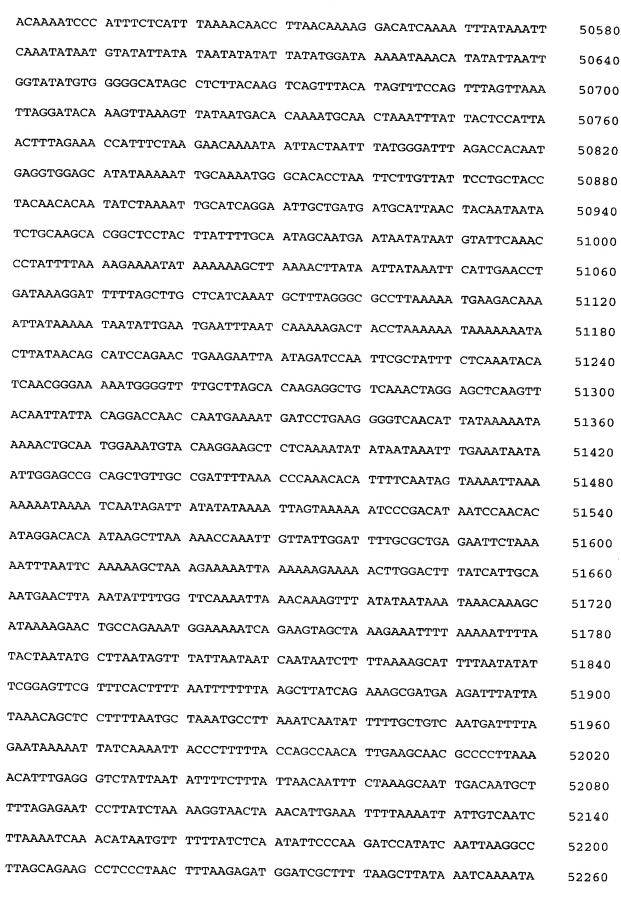
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TCAACAGCGG	ACATTTTCC	AAGAGCAATA	AGTATTTCTC	TTCTAGCCCC	ATCATTTCCA	52620
GAATATTTT	CAAAAACTTC	CATCATGTTT	TTAGAATACT	CAAGAGAATT	AAGCTCTCCT	52680
AAATAATAAC	G CTGCAATAGA	TACCACATTG	CCCTCTTTAT	TTTCAAGAAT	GTCAATAAGA	52740
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AAAGCGTTTC	AATATCTTTT	ACTCTCATAA	TTTTCAAGAA	TATAATTTGC	TGTATCAATG	52860
CCCCCGAAT	ACTTAAGAGA	ААТАААСААТ	TCAAGTATTT	CCCTTTTAAG	CTCAGCATTA	52920
AAAGTTTTCT	CAAGTCTTTT	TTTAAGAGAA	AAATTATATT	GACTATCGCT	TGATTTTTTA	52980
AGAGCTTTTA	TAATGCTTGT	CACTTGACTA	TCAAGCCCAT	AAAGAATTGT	ATCGTTAACA	53040
TACTTACCAT	CTAAACCAAC	ATTAGAAAAA	TTCTCTCCCT	TAGAAGAATT	TTCTCTCTCA	53100
ACAGGCTTAT	TTTCTGTAAT	TTCGGGCAAC	AAAGGCGGAC	TAGGAAGAGC	TGGAGAATTA	53160
ACATTTTGAG	CATACACATT	AAAAATAAGT	АААААААТА	AAAAATAAAA	GTATTTCATA	53220
AAGCATCCCT	ТСТААТАТАТ	CTAAAAAGCT	TATTTATTCC	TAAAACAGAA	ТААСАААТАА	53280
ACAAAACAAA	AATACTAACA	ATTCCAGCTG	CCATTAAAAA	ATAAAGATTT	ТТААААСТАА	53340
ACCCCACATC	CCACTGAAAC	TTTTCAAAAA	AGAAATAAAT	TGCATATAAA	GGAAAAGTG	53400
TAATAATTGA	CTTTAAAAGA	ACAAATAAAA	TTTCAATTAA	ATCAATTTTA	ACTCCTCTTT	53460
ТСААТАТТАТ	AAAATAAAA	ACAATTACAC	AAATCATAAA	AGAAATAGAT	TGAGCTAATG	53520
CTAAAGCGTT	CAAACCATAA	TAATTAATAC	CAAAAACAGA	TATTGCAATA	TCAAGAATAG	53580
AAAATAAAAC	ACTCAAATAA	AACGGTGTTT	TTGCATCACG	AATAGAAAAA	TAATATTTT	53640
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AAACTACAGC	ATTACTAAGG	ATAGAAACAC	TTCCTATCTC	AAGAGTAGAT	GCTAATGCAA	54000
ATGAAATCTG	CTGAGTAATA	ATTGAAATGG	GAAAATCCAA	GAATCATACG	AAGCCATCTG	54060

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TAAGGCAATT	TGCAAACGGA	TTAAAAATT	GTAAAAACCC	CCCAAAAATT	ACGCCAATAA	54180
CAGCACTATA	A TATTCCAAAA	CGACCATAAA	ATAAGAATAT	GCTCAATATT	ATTCCAAAAG	54240
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TGAAAAAAGA	AACAGCTTTT	TCGTGCGATT	TGTTTTTTC	ATGTGTAAAT	TCAGGCAAAA	54540
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AAAAAATCAT	CATTTAGAAT	TGCGGCTCTG	ATCTTTGAAA	TCAATCGAAA	CATATAGTGG	54840
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GTATCATCCT	TATACTCCTT	TCTACCAATG	CACATAATCC	CATTATCTGT	CAAAAGAGAC	55020
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GCATTAAGTA	TGTAATGGGG	AGTGCCAATA	CCCATTACAT	ACCTTGGTTT	TTCTTTTGGT	55140
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ССАТСТАТАТ	GAGATTTAAA	ATGCACACCT	TTTAGATCAA	TTTTTCTCAG	ATCAGAAAAA	55560
GAAAACACCC	GAAATCCGCC	CGAATCGGTT	AAAAAATTTT	TATTCCAAAT	TGTAAAATTA	55620
TGAAGACCAA	CATATTTTTC	AACAGTTTTA	ATTCCCAGCC	AATATAAATT	ATGATAAGTA	55680
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GCCCCAAAG	TACCAACTGG	САТААААСАА	GGAATATCTA	CTCTACCATG	AGGAAGATTT	55800

			189			
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TCCCAAATAA	TATATATTT	ТАТТТССТАА	СААТССТАТА	AACAAAAAA	TTGATAATCA	55920
TATAAAAAA	' AGTTGTAAAA	GAACTTGCTA	TATATATATG	CAAATAGCCT	AGATCCGCTA	55980
AAAATTAAA	AATTACAATA	GAAATAACAT	AAACAACAGC	AAAAGCAATG	СТАТТТААТА	56040
GGCTGAGTAT	[°] А ААААТА ТТТ	TTTTTAAGAG	CAAGAGCAAT	AAACCCAACA	GTAAAGCTAA	56100
GAAGAATCAA	тстааатдаа	AAGAATATCC	ТАТТТААТАА	АТСАААААТ	GCATCAGAAT	56160
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CATCAAGAAC	ATCGTAGGCG	TTCTCCTTAA	TTTTTTTACC	AACCTTAACA	AACTCTCTAA	56340
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TATCATAAGA	TTTGATATTA	TAAATTTCTC	TAGCAAAATC	CCTTATTATT	ATAGTTTTAT	56520
CCCCAGATCT	ACTGTCGCCA	ATGCTATTCT	TAATAAGAAC	ATCTCTTCTT	GCTATAGTAT	56580
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CATCTGAGAA	TGCCTTTGGC	АААТАТАААТ	AATAAATATA	AAGAATATCC	TTAAGGCCAA	56820
TATTCTTTTC	AAGATAGTTA	AGAAGATTAA	CAAACAAATC	ACCAAGCATA	ATTAAAATCA	56880
TGAAAAGCAG	GTTCATGGAC	AAAAAAGTAA	GAATGATGCT	ТТТТАТАААА	AGCTTATCTA	56940
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TGAAAGTGGT	AAACTAATTT	TTTGATAAAA	TTCAAGATTA	AACAGAGCCA	AATTTTGCTT	57240
CATGCTTCTA	TCTTGATAAG	GTTTGAAATT	TAAATTTAAA	TTATACATAT	AGTTTAAATT	57300
TTCAAAAACA	TAAGATTCAT	ССАСАТААТА	GTTTTGATTG	TATAAATAAT	TTAAATAAAG	57360
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CTTATCTGCA	TAAAAATAAT	CATAAAATCC	ACTCTCACTG	TCTGTTAAGG	CAATAGATAG	57600

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CATAAATAT	Г СТАТСААААС	CCTTAAGCCC	AGTGTTATCA	AAAAAAGTTA	САТТТТТАТА	57720
ACCATTTTC	GATTTCTCAC	CAGAAACAAA	AATCAAATCT	CCATATTGTT	TGCTTGAATA	57780
AGGCTTTAAT	ACCAAATGGG	GAACTTCTTC	ТТТТАТТТСА	TTAAAAATTT	TTAATCTGCC	57840
AATAGATCC <i>I</i>	AGTGGAAGTA	AAATATCATT	GGATATAAAA	GATACAAAAG	СААТААСТАТ	57900
TCCCAATTTA	AAAAATGGGA	CAAGTAAATC	AAAAATTGAT	ATGCCAATTG	AACGAAAAGC	57960
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AAAAAAGGGA	ACATAATTTT	GAAGAAGTAT	TCTCATAAAG	AATAAAATTT	GATTTATAAA	58140
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CATTATTGGG	TCCAAAATAA	TCCCAGTTGT	CATTTTCAGA	ATCATAAATC	AATAACCCAT	58380
GATCAAAGGT	TGCAAACAAT	AGCTTTTTAT	CTTTAATCTC	CATATCCATA	AATTAATTAA	58440
CATCAATATT	ATTGGCAATA	ACGTGCTTTT	TGTAACTATT	TTTATTTAAA	TTTAATTCAA	58500
AAAGACCCCC	ACCATATGTT	ССААСААААТ	AACTATCTTT	ATATTCTTTT	ATAAAATTAA	58560
TATTTTTTC	ATTATCATTT	TTGCTAAAAA	AATCCAAATG	TTCAATCTTT	TTCAAATTAT	58620
CGACATTAAC	АСТАТАААТА	GCCTTGTCAA	CTGTTCCAAC	ТААТААТААА	TTTTTTAAAC	58680
TATCAAAGCA	GAGTGAAGAA	ATTTTATTAG	ATCCAAGCGG	TATATTTTC	CAATTTTTTA	58740
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GCAAAACTTG	TACATTGCTA	AAATCAGCAT	TACCGGGAAC	ATTTATTTGC	TTTAAATCCC	58860
CATCAACATC	ATCTATATAA	ТАААСААСАТ	TTTTACCACC	TTAAATATAA	GTTCCATTAT	58920
AATCCGCAAA	ACCCCTAATG	CCATTTAAAA	AAATGCTTTT	TTTATCCTTA	AGATAGACTC	58980
TACAATCATT	ТТТТТТААТА	ТТАТАТСТТА	AAAGCCCTCC	СААТАТАТТА	GTTACAAATA	59040
TATTGTCATT	AAAGACAAAT	GTATCAAAAA	CGCTGTTGTC	AAGAAATCCT	AAAGACTCTA	59100
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CTGAGATAGA	AAATTCATTA	ATCTCTTTAA	ATGCAGAAAT	TGCATCAGAT	TTTTCTTTAA	59220
CAAGATATTT	TAATTCAGCT	AATCTTAAAC	TAGCATGAGA	ATATTTATAG	ТСТТТТААДА	59280
ATAGATCAAA	ATTATATTCG	GAAAGATCAT	AAAAACCATT	CTCATAATTT .	ACATATCCAA	59340

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			191			
					GTTACTATTT	59400
					CTGGCTTTTT	59460
					TCATTATCTT	59520
TTAATCCTAT	' CAAATAGTC1	CTTTTAAATT	TACCCTCATT	ACTCCCAAGA	ACAACATTAT	59580
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CAAATCTAGA	АТАТСТАТТА	CTATTCCCAA	ATCTTCCAGA	ACCATACTTA	CTGTCTCTGG	59940
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ATAACAAAAG	CAATTTATCC	TTTTCGGGTT	ATTTTTTAATA	ATAAATTATT	AAATTGTTTA	62340
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			•			

			193			
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GAGAAACATA	ACAACCGGCT	ATTACCCCTA	TTTTAGGAAC	ATTTATTACA	GCTCTCACTT	63900
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CTTGTCTTTT	AGAACTGATC	AATTTTGCTT	CTTTTTCAGT	TTTAGTTACT	TGAAAAGGAT	64380
CCCCGGCTTG	AGGCATTGAA	GAAAATCCTA	AAACACTAAT	GGCTTTAGCG	GGTCCAACGC	64440
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CGCGCCCCAA	ATCAATCTTG	GCATCAAGCA	CTTTTCCAAT	AGCTCTTTTG	GATGGATTTG	64620
CCTTTAACAA	CATCATATCT	GACTGTAAAA	GAATCATATC	AAGTAGTTCA	GAAATTCCTA	64680

TATTTTTAAG	AGCAGAAATC	АТСАСААААА	TAGTATCTCC	CCCCCAATCC	TCAGATACTA	64740
AACCGTATTC	TGAAAGCTGG	TGTTTAATCT	TATCGGGATT	TGAATCTGGT	AAATCAATCT	64800
TATTTATAGC	AACAATAATT	GGAACATTTG	CCTCTTTTGC	ATGATTGATA	GCCTCAATGG	64860
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CCCCACGACT	TCTCATCATA	GTAAAAGCTT	CATGACCAGG	AGTATCTAAA	AATGTTATTT	64980
CTCGATCATT	АТАААСААТА	GTATAAGCTC	CAATATGCTG	AGTAATACCA	CCGGACTCTG	65040
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GACCCATTAT	TGTAATAACA	GGAGGCTTTT	CAACTCTTTT	GCTTTGATCT	TCCACTTCTT	65160
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CTAAAATAGT	TGCAGTATCA	GAATCTATCT	TTTCATTAAT	AGTAACCATT	ACGCCCAAAG	65280
CCATTAATTT	AGCAATCAAA	TCAGAAGATT	TTAAATTCAT	CTTTCTTGCA	AGATCAGAAA	65340
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CACCTCTATT	ATCCCTATTT	TGTGAATACC	CACCAGTTCT	GTTGTCTCTG	TTTTGTGAAT	65940
ACCCACCAGT	TCTGTTGTCT	CTGTTTTGTG	AATACCCACC	AGTTCTGTTG	TCTCTGTTTT	66000
GGGAATATCC	ACCAGCTCTA	TTGTCCCTAT	TTTGTGAATA	TCCACCAGCT	CTATTGTCCC	66060
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TATTTTACAA	CCCGGACAGG	AGGTCATATT	ТТСАТТААТА	ACAACACCGC	ATTCAGGACA	66360
AAGAAGCTCT	TCATCTTCTT	CTACCTTTTC	CATAGACTCA	TCATTGTCAT	TAGCAATTAT	66420

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ATTAAAAAGC	ACTCCCTCAT	CTGCTTGTAA	AAAATTGTTA	ATATCATCAA	ACCCCTCTTT	66540
TGATAAATTA	GAAATCACAG	AAGGATCAAG	CAATTTAAGA	TCACTTATTT	TACTAATCTC	66600
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GAACTATTTG	AATTTTTCCA	TTATTTTTAT	TTCTAAAGAT	ATTAATTTCT	AATATCTCAA	68100
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TATCTCTCTG AAT	TTTAAGCT A	GAAAATAGA	TTCAAACTTC	САТТААААТТ .	АТСТТТТААА	76920
TTAAATTGTC CAT	TATCCTTG C	AAATTTGAA	AGTTTGTTTA	TAAGTTTAAC .	ATCAGAAATG	76980
TACAATTTAT CAT	ГАТТСАТА Т	'AAGCCCTTA	AAACCAAAGT	TGAAATTATA (GGCAGGTGTT	77040

			201			
TTAGAAACT	TTATTATATT	AAACTCGTCT	ATTTTAAATT	TCAAATCTTC	ATTAAGGCCT	77100
AAATAGTTC	С САТТААААТТ	TATATTTATT	AAAAGATCAG	AGGTTTTATT	GTAAACCTTA	77160
AAATCATTA	A CATTAAGGGT	ATAAACTACT	TTAGAATCAA	AATTAATTAA	ATCTAATTTA	77220
ATACCAAGAC	GAGATTCGGC	AACAATAAAC	TTATCTTTAA	GATTAACATT	AAAATGCAAA	77280
GGATAAACTT	TATTCAAATA	AGAAAAATTC	GTGCTAATAT	TAAACCCACT	TTCAAATAGT	77340
TCAACAAACA	A AGTTAGAATG	CAAATTGTGA	TCATTGTACT	GCAAATCAAA	ATTGTTTGAT	77400
TTGTAAAAAT	TTTTTTCTCC	ACTGGCATCA	AGCACAAATT	TGAAATTGTC	TAACTTTGAA	77460
AATACCATGA	AATTGAATTT	ТТТТААТТТА	TTTTTATGAT	AATTAAATTT	АТТААААТТА	77520
AAATCAGAAA	CCAAATTTAA	ATATTTACCT	GAAAATAAAG	TCTTGGGAAA	AAAATTTATC	77580
AAGTGAGAAC	TGGGAATAAC	TTCTTTTAAA	AAAAGCAAAG	GAAATTCTTT	AATACCTAAG	77640
CTTAAAGAAA	ATTCTTCATC	ATTAAGATCT	CCTTTTAAAG	AAATTTGAGA	GTTTTTATTT	77700
ТСТАААТААА	TCAAATAGTC	ААСАААААТТ	TTATCCTTTA	AAAAATAAGT	ТТТТААААТТ	77760
AAATTTTGAA	AACTAAGATT	TCCAAGACTA	AAATTATCAG	ACTTAACCGA	AAAAATATCT	77820
TTATCTTTAT	ТААААТСТАА	ATACCCATTT	AGGTCGTTAA	AGTTTAAAAT	TTTTGCAGAC	77880
TTAAAGTTAA	GACGTCCCAT	TGGAAGCAAA	TCTTTCAAAG	AATAATAACC	TTTATAGTTT	77940
ACAACCCCC	TTTTAAGCTT	TAAAAAAGCA	TTCTTAACAC	TTACAATTCT	ATCATCCCCC	78000
TTGATTTCAA	GCTGCAAGCC	TTGAACTTCT	TTTCCTATAG	TATCTACATT	TAAAGATGAA	78060
TCTATTATTC	CTGCATATCT	TAAATCTTTG	ТССТТААААТ	CATAAGAAAA	TGCCAATTGC	78120
CCATTTAAAC	TTATATCAAA	ATAATCTTTA	TAAATTTCAA	AGCCTTTGTT	TAGCTTAATC	78180
СААТСТАААА	GACTAACATT	GAAAAATAAA	GCATCTAATC	GAACAAAACC	ATTAGCCTTG	78240
TCATAACTTA	AATTAAAATC	AAAATTCTCT	CTTCGTAAAT	ТАААААТТТТ	ТАААТТТССТ	78300
TTTGAATAAT	TTATTTGGAA	CCCCTGCTCA	AGTAAAGAAA	AATAACTTGT	ТТТАААТТСА	78360
AAAAAGCTAA	AATTAACATA	GCCATCTTCA	AAGCCTTTTT	TGAATTTCCC	CTCAAAATAG	78420
AAAGTTGAAT	CCAAAATTCC	ATCATCAACT	CTTTCAAAGG	GTAAATTAAT	ТТСТАААТТТ	78480
TTAACAGCAC	TAAAATCAAC	TACAGAGCTA	ТАААААТАА	CTTCATCTAC	GGTACTTAAG	78540
GAAAAATTTT	TAACTTGAAA	ATTAAGCCAA	СТАТТАТСАТ	TAAGCTTGAT	ATTAATATTG	78600
ATATTTTCTA	AATTAATATT	ТААТСТАТАА	AGGTAGTTTA	AAATTTTATT	AAAAACTGTA	78660
TTTTCATTGT	CAGAATAGGC	ATTGCTAGGA	TTTAAATCGC	CAGATAAACT	AAAGTCGTTT	78720
АТАТСААААТ	TGAAATTACT	TCCTTTAACA	ТАААСАТТТА	TTATAATAAA	TTCATCACCC	78780
AAAATTAATT	TAAACAGATT	TAAATCTATC	СТААСААТАТ	СТАТТААТАТ	TTTATCTTTT	78840

CCATCCAAGC	TTAACTCTAA	ACCGTCTATC	TTGATTGATG	ATAAGAAATA	CGGTGAAATT	78900
ТТАТСАТАТТ	' ТААТСТТААА	GCCAAATTTT	GATTCAAGAT	ATTTTATAGC	AAAAAACTTT	78960
GCAGAATAAA	TTTGAGCTTG	AACAAATAGA	TTAATGGAAA	AAATTATTAA	AACAAAAATA	79020
AAAAATGGCA	AAATCAACAA	TATAAATGTC	TTACTTCTCA	AAAACAACAA	ATTCATACAC	79080
TCTATCGATA	ATTATTATTA	ТАТААТААТТ	ATCGATAACC	TAATTATTGA	CACCAAAAGA	79140
AAGGAAGAAA	AAATATTTGT	GATTAAAATA	TTGAAAAACT	TTTATTGCAT	AGAAGGAATT	79200
GATGGAAGCG	GGAAAACAAG	CATCACTAAT	AAACTAAAAG	CTCTTTGCAA	CGATGAATCA	79260
AGGTATTATT	TTACAAAAGA	ACCATCAAGT	GGAATAATTG	GAGAAATGAT	AAGAAAGCAA	79320
TTAATGAATT	TTGAAAATCC	TTTAGAAGAA	TCAACATTTG	CATATCTTTA	TGCTGCAGAC	79380
CGACACGATC	ATTTATATAA	AAAAGGTGGA	ATACTGGAAA	TTTTAAACAC	AAAATCTAGA	79440
AAAATAATAA	CTGATCGCTA	TTTATTCTCA	TCGATTGCAT	ATCAAGGAAA	ATTAGGATAT	79500
GAATTAAATA	AAAATTTCCC	ATTGCCTGAA	AAAGTATTCT	TTATCGAAAC	AGACCCAAAC	79560
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AAAATTTTCA	АТСТААТААА	ATTCTAATAT	AATTAATCAT	ATGCATATTT	TCAAAAATGT	79800
CCCCTTCCAA	ATAAATTTAA	TTTTATTTCT	TTTAGTATCA	GTTGCAAAGA	TAAATGCATC	79860
GTCCAAATTT	TATTACGCAG	AACAATGGTA	TGTAATTTTT	AATTCTCAAA	TGAAAAAAA	79920
ACCTGAAAAC	ТАТААААААА	ATATATTTTT	TCTTCAAAAA	GCCTTAAAAT	ACCCATTTGG	79980
AAATCCAAAA	TATTCTCTAA	CTAAAATAGA	AACCAAAGAA	CAGTGGGAAA	ААТАТАААСТ	80040
TCTTTTCAAA	ATGCATGTAA	ACTTGCTTCT	AGTTAGGCAA	AATTTACATT	TAGGAGATTT	80100
ATTCGACACA	AGAAATTTAT	ATTTTTTCAA	AACTCCAGAA	AAAGATGGAA	TTATTTCCAA	80160
TCTAGAAAAA	TCAAAAAAAT	TATATAAACT	AGCTATTAAT	TACTACAGCG	AAGCACTAAA	80220
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CTGGGAAGAT	GAATATCATA	AAATTTCTCT	TAAAGAGCTT	AATTACTATG	ACATTATTAA	80340
AAAAGAACTA	CTAAGAATTG	ACGAAACTAA	AGCATTTTTT	GAACAAGGGC	САААСТАТТА	80400
TTAAAAAAAC	TCTTTGCCCT	CTTTGGAAAA	AAAAATTTTA	TAATATTT	CCTTATTTAA	80460
AGAAAACTTA	AAAACAAGAT	СТТТААААТТ	ATCCTTACTC	ААААТАСТАТ	ATTCTGAGAA	80520
AAGAGTTATT	AAGGCTCTTT	CTGCTAAAAA	AGGCAATTCT	AAAATATTTC	ТТААААТТТС	80580

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GGCTCTAAAT	TCACGCGCTT	TTTCACTATC	203 TAAAGAATTT	ACAAAATTAG	AATTTTCAAC	80640
ATCAGTGCTT	AGTGCTACAA	TTTCATTTTC	AAGAAATTTT	ТТАТСТССТТ	GTGAATATAG	80700
CAAAGCAAAT	GGCTTTAAAA	AAGAAAAAA	ATATTCCTTA	CCTATAAGAT	AATGGTGCAT	80760
TGAACATCTT	GTAGAGTAAT	TTGGGTAAAT	AGCAGATTCA	ATCTCTTCAT	CGCCACCAAC	80820
AATAAGCAAA	GGATCAAAAT	AAGGAGCTGG	AATTTCTTTA	TTGTTGTAAA	AATAATACCT	80880
ATACGAAAAA	AAAGATTCTT	CCATGCAATC	AATGTGCCCA	CAATAAGCTC	CAAGCTTATA	80940
AATCTTATCT	GAATATTCTA	CTAAAAGTTT	GGCAGTATCA	TTGAAAGATT	СТТТТСТААА	81000
ATTATAAAGC	AGTGTAGGTA	АТАТАААТАА	AATATTCTCA	TTTGATGAAA	TTTTATTTAA	81060
AACAAAAATT	AAACGTTCAT	САТАААААСА	TGCCTCATCA	ATAATAAAAG	TGCCACAACT	81120
AGGATTAGAG	GCTATTAAAT	TTTCAATATC	AAAAGAGTTG	CTAGCATAAC	CAATCTCATC	81180
AATTTTATCT	TTTCCACCGC	CTCTATATGG	TATTACGTTT	TCTGGATAAT	CTTGAAACCT	81240
CCTCTTGTCG	AGAAAATTTC	ТААТААААА	TACATTAACC	СТАСТТСТАТ	TTCCTTTAAT	81300
AATATTGCCC	AATACCTTGA	AAGATTTTTT	TCTTACAACA	AGCGAATCTT	ТАТАААТТТ	81360
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TACCCTAAAA	TCAAAATGAC	TAACAGAGAC	AATGTTATTT	AATTTAGTAT	CTTCTTTATT	81480
AGCAAAGTCT	AAACAAAAAC	CCAAAAATCC	TCCCTAAAGT	АААТСАААТТ	СААТТАТАТА	81540
AATAAAAACA	ACAAAAAACA	TTAACATTAA	AAGCCTAAAA	ATTAATAATT	TAGGATCTTA	81600
TTAAAGCTAT	TATTCAAAAG	AATAATAGCT	ТТСААААСТА	TCATCATCTA	ACAAAGCTTT	81660
CTTTATTTT	AGTTTATTCT	TCTCATAAAT	ТТСААТАТАА	TTAAATTTT	TAGAACTATT	81720
AACTTTTTTA	TAAATTGAAA	CCAAACTTCC	AACCACATAA	TTTTTAATTT	CTACCAAATT	81780
AGATCCAAAA	TATTTTTTT	TACTTATCAA	GCTTGATCTA	ATATCCAAAA	CAGAAGTTTT	81840
TTCAAAAAAT	AAATTTAAAG	CATTTGGAAT	ААААААТСС	СТААТАТСАА	TCAAGAACAA	81900
CTCTCTGATC	CCAAAACTAT	TAAAATTGCA	GCCCAAATTG	TTAAAAAGAT	TAAACTTAAA	81960
AGCATGTAAA	GCAAAGGTAT	AAACATCTCT	TTTATCAGGA	TATTGAACCT	СААТСАТАТС	82020
AACATAAGGA	TAAACAGAAT	AATTTATTT	ATAACCAAGC	AAACTATTCT	CATAATAAAC	82080
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GTCAAAATCT	' ACTATTCCTG	AAAAAATGCC	ТАСТААААСТ	CCATCTTTA	GTATGGCAAC	82200
ATTATTTTA	TTATCAATGC	AATAAATTCC	TGACAAACTT	ТТАТААТСТТ	СТАААААТТТ	82260
ACTCTTCATG	TCGGGATCCT	CTAAAAGATC	ATAAAACATT	ттататтсат	TTATTGTCTC	82320
AGGAGGAAAT	TTTTTAAAAA	TCCTATAAGC	TTCATCAGGA	TCTAAAAGTT	TGTATTTTAA	82380



			205			
CAACTAACAG	CTGATTAAGA	GTTTGCTCTC	TTTCATCATG	ACCACCGCCA	AGCCCCGCAC	84180
CACGACTTCG	ACCAACAGCA	TCAAGCTCAT	СААТААААТ	AATACATGGA	GAATTTTTTC	84240
TAGCATTATC	АААТАААТСТ	CTAACACGAC	TTGCTCCAAC	CCCAACAAAC	ATTTCAACAA	84300
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GTAAATTTAT	ATCAAGATAG	GGAATGCTGG	TAGAAAAATA	AGACTTTGCA	AAGTTAGAAC	84780
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CCATACTAAG	TTTAAAGTAT	ТТАААТСААТ	AATCCCAATT	AACCTGTTAT	CTAATGCTAA	85140
CAACATTAAA	TAAGCCGGAT	TACACCTTAT	AAACTTAGAA	AAAAATTTTT	TTGCTTTCAA	85200
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TGCAATTCCT	TCTGAATTTA	AAATTTTAAA	AATCAATCTA	AATACCAAAT	ACTTAGGAAA	85560
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TTCATCTTTT	ССААААТААТ	CCGCAAATTC	CTTTGAAAAT	TCAGATATTC	TTTTAAGACA	85680
TTTTTCATAT	ССТТТААААА	CCTTTTTTAT	AGCGGGTAGC	AAATTATTTC	TAACCCTATT	85740
TCTTAGATAT	AAATTTTGAG	CATTTGTACT	ATCAACAAAA	AACCCAATAT	TATTCAAAGA	85800
TAAAAAATTT	TCAATTTCTA	GTCTTGAAAC	CTCAAGCAAG	GGCCTTATAA	TGTTTCTATT	85860
GACACTAGGA	ATACCTGAAA	GACCATCCAA	AAAAGATCCT	TGAAAAAATC	ТСАТААТТАТ	85920



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TATATATTCC	TTAAAAATAG	AAGTTTGCAA	AGCTTTTCTA	AAATCCTGAC	TAATAGGATG	87720
TACAATGTCT	TTATATTCAC	CGACTCTAGT	TCTTCTGTTA	GGCATCGCAA	TAAATACTCC	87780
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AACATATGCT	AATAATTTAG	AACCAGAATT	TTTACTATCA	ACTTTCTTAA	TCCTTATGTC	87900
TGTAATATCC	ACTTATAAGC	CTCCCGCAAA	AAGTACATAA	CTTAAATCTA	AAATATTTTC	87960
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CCCTAGATTT	TTCACTCATT	AAATGAATTA	CCAAATTTGC	ACCAGAAACA	ACAGTCCAGT	88140
CATAAACCAA	CCCTTTTCCT	TCAGCATTAA	GATTAATTTT	ТТТТТСТТТА	AAGAATTTAA	88200
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AAAAATCAGT	CCAATTACAA	ATATCGCTAA	CATTAATGCC	TATAACATCA	ATTCCATTAA	88320
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AATCTTTTAG	CTTGAACCTC	AGAAATTGGC	TTAATATTTG	AAGTTTTAAT	TACCTCTCCA	88500
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CTGTCATTTT	CAATGCCAAA	ATCTGAAATT	TGAAAAAGAA	GTCTTTTAAA	AAATTCTTTA	88980
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CTTTCCTAAA	TAAAATCTGA	ТАТССААААА	CCAAGTCTTA	AAAATAAAAA	GCCCACAATA	90180
AAAATCAATT	ТТАТТААААА	GTTTTAGCCA	AAATAAAAA	TTCTTTAATA	AGTTCATCAA	90240
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GCACGCTCAA	ACTATTACCC	GATTCTCCAG	GTTGAGCAAA	CCTTGGAACC	CTTCTAACTG	90780
AAGTTTTAAA	ATTCCAATTA	CCAAGACCCC	CTCTGCCACC	TTTTAAAACA	ACAAATTCGT	90840
CATTTAAATT	TTTAAGCCTA	TACAAAAGAG	TTCCATCATT	TTCATTATAA	ACTTCTGTAT	90900
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GATTTTCCCT	CACCTTGAAA	ATTACACTCC	CACCACTCCC	ACCGTTTCCG	CCATCTGGAC	91080
CACCTTTTGC	ATTAAACTTT	TCTCTTAAAA	AAGAAACACA	CCCAGAACCA	CCATTGCCCG	91140
AAACTACCGT	TATATTTACA	GAGTCCTTAA	AGTTATACAA	ACTTTCTCCA	ATTTTTCAAT	91200

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TAAAACCAAA AATCTCCA	AT CTTTTCAATT	AAAACTAAAC	AATACTTACG	TATTTTCGCC	91260
CCTTTAAAGT TTTAAACT	CT ACCTTACCAC	ATGAAAGCGC	AAATATTGTA	TAATCTCTTC	91320
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ACCATTGGCT AAAAGATA	AA TAATTACATO	GTCTTTTACT	TTTACCAAAA	CATTAATCAA	91800
TATACTTAAA AAACTATT	TC ATCAACCAAA	. ATATAAGAAT	AGGTTTGCCT	GTGCCCAACT	91860
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TCTTCTTTAT AGGTACAT	CT AATAAGAGAA	TTTACGACAT	AAGGCTTTCC	TATTTTAACC	91980
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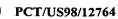
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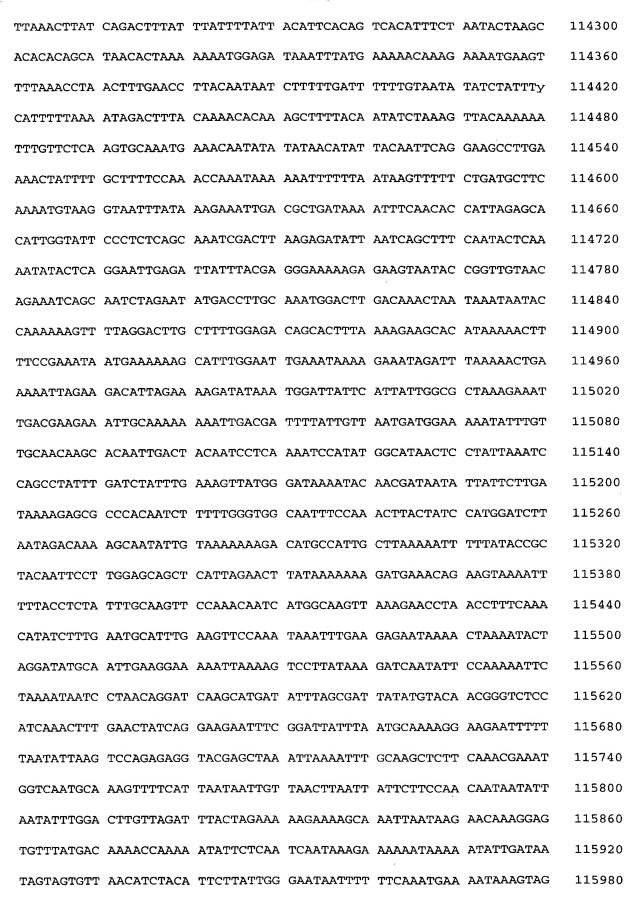
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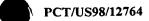
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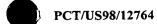


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	CAATAAGAAG	AGACCCCTTT	TGAGTACCAT	CCCCGCCAAT	GTTAAAAATC	ATATTAATGT	144840
	TCATTCTCTC	TAAAGTATCA	ACTATTTCCA	CAGGCTTAAT	ACCACCCCTT	GAAGAACCAA	144900
	GAATAGTACC	ТССАААТТТА	TTAATATCAT	CAACAACATC	TGGATTAAGA	ттаатаааа	144960
	GTGAATTTGA	CTCAGGAAGA	AGCCCTTGAT	ATCCAAATTT	TACTCCATAA	ATATTGCGAA	145020
	CCCCATATAT	TTTCCATAAA	GTTCGCACAA	TAGAGCGAAT	AACATCGTTA	AAACCAGGAC	145080
	AAAGCCCACC	CACAAGTAGTA	ATAGCAGCTI	TAACATGCCT	GGGCACAAAA	TTTTTTAAAT	145140
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	TATATACACT	T AAACTTGATI	TTATTTTTT	CATTAACAAA	ATGGGAAGAF	CCCTCACTAG	145260
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	СТАААТТТТ	ATTTTAAT	CTATACACC	A AATACTCCTI	TATAGAATTA	A TAACCTAATT	145380
	ATTTTCTAA	r aaatcgact	TGATCTTTA	A TCATATCGT	A TATGTCATCO	G TAAATATAAG	145440
	GAGACCCTT	C AATAGGAGA	AAATTAATT 1	r TACCAGCTAT	r gaattcaaa	а татттаттса	145500
	ACTTTGAAT'	r TTTCTCAAA	A TCAATAAAT	G GAACTCTAT	r ATTAATAGC	C TCTCTGAAAC	145560
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СААТААТАА	C AAATGTTTTC	ATATGCTTC	ACCAACCAAA	ATATCTTGCC	TTGGCCTTGT	147180
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ССАТТТАТТТ	GCTCATTTGT	TCTTGTTCTA	ATAGATATTC	TCTCTTCTGT	TGCTTCTCTC	151260
TCACCAATTA	TAAACATATA	AGGTATTTT	TTAGCCTGAT	ATTCTCTAAT	TTTAGCATTC	151320
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		`	243			
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ACTATTTCA	AAACCATCTA	TTCCAGTTTG	ACCAGTACCT	GTTTTTCCTC	CAACCTCAAC	154620
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TCTTTAAAAG	ТТАААААТАА	TCTAGTAAAA	TAATTTTGAA	TTGGATATAA	AAAGTTAATA	156240
GACATTATAT	TTACAAAAAG	ATCAAGGTTG	AAAATTGAAT	AATTAAAAGA	TTTTAAGTCT	156300
ACAAAATCAT	AAAACACAAT	AGCTAAAAAC	САТААТАТАА	TTTTTGAAAG	ААТААААААТ	156360
ATTGTCATGC	TAAGCATATT	TTTGGGCATG	AATAATTTTA	TTTTATTGTT	ААААТААААТ	156420
ATTATCGTAT	ACCCAAAAAC	AAAAAATCCA	AGTGGTAATC	CTGTAAAATA	ATCCATAAGA	156480
AGACCATATA	AAATGCTAGA	ТААТААТССС	ACATTAAAAA	ТААААТТСАА	AGAATTAAAA	156540
ACTAGAAAAA	ТТААААААТТ	ATCTATTGAA	АААТААААТ	AAGTTGCAAA	ATAGTGTTGA	156600
AAAATTTTGC	CTAAAAATGC	GCTGGAAATA	AAATATGTAA	AAAATGTTGC	CATTATTCAC	156660
СААТСТСТТТ	GTTGTTTTA	ACAAGAAAAA	CATACTCAAG	СТТАТСТААА	ACTATAGCTG	156720



GCTCTACTTC	TATTTTAAA	AGAGAATTA	T AATCAAGAA1	T ATGAAAATTI	GTAATCTTTC	156780
СААТАТАААТ	ACCAACTGGA	TATTCACTA	ATCCAGCAGT	AACAATAGAA	TCCCCTATTT	156840
TTAAATCTTT	TTCAGCAAGT	CTATTAACG1	T AATTCATTTC	AAGTTTTTA	CCATAACCAT	156900
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GGCCACTAAA	TCCATCCTGA	TATGCAACTG	CTATCATATC	ТТТТТСТАТС	CCATCATTGA	157080
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CATCAAATTC	GTCACCACCA	GTCCTAATTG	CTCTACTTAC	AACCATGCCG	CCAAGAGAAA	158040
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CAACCGCAAC .	ААСТТТАТТА	CCTTTGGTTA	TATCTATTGC	AACAACAGAA	GGCTCGCTCA	158460



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TATAATAATC (CGGACTACTC	TCTTTATCCT	TATCTTTTTC	TCTTTTAAAA	AACTCTTCTC	162000



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	`	•	249			
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CCTCATCACT	TTGAAAACCA	TCATCTAAAA	TCATAAAATT	TCTATCAGAT	TCAATCTCAA	162360
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TTTATAGGTA	ТССТТТАААТ	TTTTTTTTAA	ATCCATTAAT	GAAAAATCTT	TATTATTTTC	162900
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АТТТАААААТ	AAATTAATCA	TGGCATTTAA	ATCTACAGTT	ТТАТТТАААТ	ТАТАТТТАТТ	163260
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TCCAGCATCA	TCCCCATCAA	AAGAAAATAT	TATCTCATCA	GCATATCTTT	GAATTAAAGC	163500
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CTCCTCAAAA	СССТСАТААА	ATCCATAAAG	AAGCTCCCTT	ТТТТТААААА	CTTCAGTTTC	163680
АССТАААТТА	ATATACTTAG	AACCTTTCCC	ATCTAAATCT	CGACCTCCAA	AACCAACAAC	163740
GTTTCCTTTA	AAGTCTTTAA	TTGGAAAAAT	TAATCTTTGA	AATAAAATAG	AAACTTTGGG	163800



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	AG ATATTGCTCT ACTCTTTAAA ACATAATCTA AAGCTT	
	TT TAATGGTATT AATTAACCGA GAATTCAAAG AGTAAA	
	TT CATTTTTATT TTCACTTCCT CGACTTATTT TTAAAT	
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	C GCCTATAGAC TTAAGCTTAT TCAAAAATT ATCAACA	
	I TTCTATACCC TTATAAAATT TATAAGTATC TGGAAAT	
•	A ATCAAGCCCA AGCTCATAAA TAAATGATTT TTTGTTGA	
	C ATCATCAATA ACAGAAAATT CCTTAAGCTT TAAAGCAA	
	C GGGTATTGTA ACATCAATAT TTACGTTAGA AGATCCCT	
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						АТААТАСТТА	165960
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			' ATAAAAAGTG				166260
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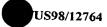


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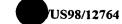
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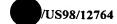
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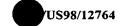
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GATCCTAGTA	TAAACTGGCC	TTCAACCCCA	АТАТТАААА	GACCCGCTTT	TAAAGAAATA	193860

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			267			
CCAATAGAAA	GACCTGTAAA	AATCAAAGGA	GCTGAATAAC	TTAAAACATA	ACCTAAATGT	193920
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CTTGTTTGTA	ATCAAGAAAA	CCAAATTTTG	AATTTTCATA	ТСССААААТА	ATGTTTTGAA	195420
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			269			
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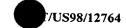
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AAAGATTGAC	CTTAACATCA	AAAGATTCAT	TAGATTCATT	ATAATCACCA	TTATTAAAAG	205380
AATCATAAAA	TTCTCTTGAA	AGATTTACAT	AATAAACTCC	ATTCTTTAAA	AAAGAATATA	205440
AAAATCTTGA	ATCACTTAAT	AAAAACCCAA	AAGAAAACCC	TTCATTGCTT	CCTAAAAGAA	205500
AATCTTTTAC	TAAAAGATCT	AAATTATCTT	TCAAATTTTG	TTCATCTCTT	AAATATCTTA	205560
AATTAGCAAC	AAATCCCTTG	CTAGAATGAA	AATAAAAAAC	CTTTTTTGAA	AAAAGATTAT	205620
CATAATTTAA	AAAAACCATA	CAAATAGAAA	ACAAAAAGCT	TACTGCCAAA	GACCCCAAAA	205680
GCACCCTAAT	CATATGCTCT	TTTTTTGAAT	TTAAAAATTT	АТАААТСАСТ	ACATTATATT	205740
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ATATTGGATA	AAAACCCCAT	TTCAATCAAC	ACAGCAGGCA	TACTGCTGTT	TTTTATTACA	205920
AACCATTGCT	CTTTTCTGAT	TGGCCTAATA	TTAGTTTCGC	TTAACTCATT	ТТТАААСАСТ	205980
TTATACAAAA	TTTCAGCCAA	TCTTTTTGAT	TCATATTTAT	АТТТААТАТС	TAGTATATCA	206040
TTAAGCTCGC	TTAAGTATCT	ATTACCTTTA	АТАТСАТАТС	ССТТААААТС	ТТТААТААСТ	206100
TCTCTTTTTG	AATCCTTAGG	AAGATACCAA	AACTCAACTC	CTCTAGCTTC	ACCGTTTGGA	206160
GCATCATTAG	CATGTATAGA	ТАААААТАТА	ACATTATTGG	GGAAATTTGG	CTTTATTGCA	206220
TTTGCAAATT	CCGACCGTTC	TTTTAAAGTT	АААТАААСАТ	CATTTATACG	AGTTAACAAA	206280



ATA	TTTTTAT	ТТАСААААТА	ATTACTTAAA	ATTTTAGACA	AATATATAGA	ATAGGTTAAT	206340
GCA	AAATCTT	TTTCCTGAAG	CACAACGTCA	TAACCATTTA	TCTTTAAAGT	CACAACAGCA	206400
CCA	GTATCAT	GCCCGCCATG	TCCAGGATCA	ATGATTATTG	AAGTAATTCT	GGGTTTATTA	206460
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GCA	TATTCAA	AGCCTACCCT	AAACTTCAAA	TATCCCTTAT	CATTTTCAAT	TGTAAAAACA	206640
TCA	ТТТТСАА	TGTTAAAATC	АААССТАААА	ACATTAGTAT	САААААААТС	AAGAACATTT	206700
AAA	TAATCGG	GGGTCTTAGA	ATACAAGCTT	AAATATGAAA	ACAAAATCAA	ATCAATCAAT	206760
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TTT.	AGTAATC	TCACCTTTTA	TCTCCTTAAA	CTCTTTTTGG	AAGAGAAAAG	GATTAATTTT	206880
GTA'	AAATTTI	CAAATTTTGC	AAAACCTTAA	AAAAGAAAAA	ACAACGCCAT	TTCCAACAAA	206940
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GTC	AAAACCT	CCAAGCTGTA	AAAATTTCTC	TTTAGAATAA	AGTCCGCAAT	AATCCATGGT	207180
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ATTI	TTAGAT	TGAATAACAG	TATATGAATA	GCCACTACCT	GGAAGACGCA	ТАААТТАСТТ	207720
TTAA	AATCCT	TATAATTAAA	ТТАТААТААТ	CATATGTTAC	ATAATACAAT	GCTAATTGCA	207780
AGAA	TAATGA	АТАТТААТАС	ATTATTCTAC	GGCATGATCA	TTATCATTTT	TGCACTCATT	207840
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AAAA	TTGAAT	ATAAAATAGA	CTCAGAAAAT	GACTTTATAG	CATTTAAAGA	ТАТАААСААТ	207960
AACG	AAAAAG	AAGAAGTAAT	CATCAGATCA	AGACTAAACT	САТАТАААА	TTCAAAGATA	208020



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					AAAAGAAATA	208080
					GGAGATTATT	208140
CATAATGCA	G AAAGAGGAA1	CAACTCTTTC	GTATATATTG	TAAAAGCAGA	AGAATTTGCA	208200
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AGTGTACGAA	AACATTTTAT	TTTTGTCAAA	ATTAAAAACA	GCATATTTTA	AATGGGTTTT	209160
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			277		_	
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АААТТААТАТ	AAAGACTTAA	CTCGACAAGA	GGTAAAAGAT	CTACTCTCAT .	AATTGGTCTT	215100



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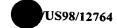
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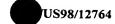
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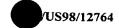
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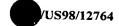
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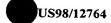
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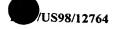
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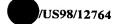
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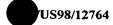


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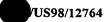
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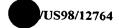
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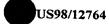
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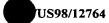
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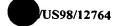
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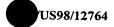
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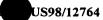


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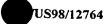
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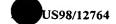


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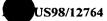


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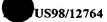
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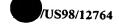
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CATTGGTCAA	ATTGGCAGCC	АТААААТАТТ	CAGGATAATT	AGCCTTAAGA	TAAGCGGTTT	315960
GATATGCTAT	TAAAGAATAC	GCCGCTGCAT	GCGATTTGTT	AAATCCATAC	CCAGAAAAGG	316020



GCTTTAAAAG T	ТСАААААТТ	TCACTAGCA	A TTTCTTTGT(ATATCCTTTC	TCAATAGCGC	316080
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GTCTTAAAAT A	TCGGCCTTG	CCAAGAGAAA	A AGCCTCCAAT	TATTTTTGCA	ACTTCCATTA	316200
CTTGTTCTTG A	ТАААСААТА	ACCCCATAAC	TTGGTCTTA	AACTTCCTTI	' AAATCGGGAT	316260
GAGGATATTT A	ATTCTCTTA	ACACCTTTTT	TAGCAGCAAT	AAATTGAGGA	ATAAATTGCA	316320
TAGGACCTGG CO	CTATAAAGA	GCATTTAAAG	CTATTAAATC	TTCAATGCTA	TCGGGCTTTG	316380
CGTCTTTTAG A	ATTTGCTGC	ATTCCTTCAG	ATTCAAACTG	AAAAACAGAC	GCACTTCTTC	316440
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CTGGATTTAC AC	СТТСТААТА	AGATTTTCTG	CATTTTTTAT	TAACGTCAAT	GTTTTCAAAC	316560
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CGGCATTCAT TA	ATTCTTTA	TAAACAGGCT	TGCTAGTAAA	ACACTCTTTC	AAAGAATTGT	316800
САТСТААААС СТ	CTTTTAAA	GAAACTTTAG	GACCATCAGG	AATAAACTTA	GTAAGTTCAT	316860
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TAGAATACTT AAC	CCAGCCTT 1	ГСАТТТАСАА	TGTCTTGATC	TTTAATACCA	TGCCTTTGAA	317700
GCTCAAGATA AAA	ATCATTG (CAAAAACTT	TTTTAAACCA	AAGAATTTCA	PTCTTGGCAT	317760



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CATCGTTCAT	GATCAATTCT	TTTAATCAAA	ACAGCATCTG	TAAGCACAAC	TCTCTCGCCA	320160
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GATGAAACTG	GCAAGCTACG	AAAAATTTAT	TTTCAGGAAT	TTCTATTAAT	TTTGCCATTT	321180
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CATTATTGAC	TTCATACCTA	TGTCTAAATC	TTTCAATTAT	CCGATCTTGG	CCATAAAGTT	321300

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	AATTCCCTTT		GTAAATGGAT			321420
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ATTCTATTAC		AAACCAAGAC				321540
		ATTTTACCTT				321600
		TTTAAACAGC				321660
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GCACAAAAAA	ATTAGATTTT	АТААСТССТА	CAAGCTTTGA	AAGCTCTTCT	ATTTTTGGAT	321840
CAACCTTAAT	ATTTAACTTA	GAGCTTAAAA	TCTCATGTAC	ACCCTGCTTA	ТАААААСАТА	321900
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TAATGTTCCA	ACTAGACTTG	GCATTAAGAT	ттааааасст	CTCGTAATGA	CCAAAGTCCA	322440
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ATCTGTCAAA	AGAAAAAATT	AAATCCGAAG	AACATGGCAC	AAAATTTATA	CCCAAATAAA	323100

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	_
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TCAGAGATAT TCCAACTAAT AATATAAATT TGCTTAAAAG AAATAAAATA	324840

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		343			
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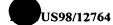


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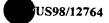
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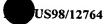


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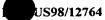
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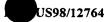
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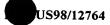
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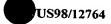


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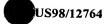
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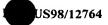
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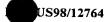


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373	
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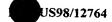
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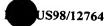
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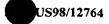
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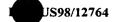
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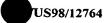
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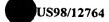
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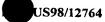
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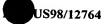
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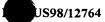
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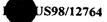
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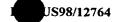
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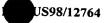
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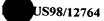
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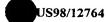
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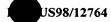
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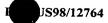
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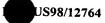
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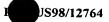
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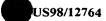
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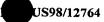


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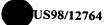
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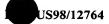


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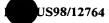
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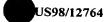
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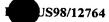
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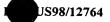
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TTTATGTTAA 2	AAAAAGTTTA	TTATTTTTTA	ATTTTTTTAT	TTATTGTTGC	TTGTTCTAGC	514260



TOTAL TOTAL CONTROL OF THE CONTROL O	
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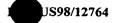


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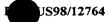
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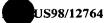
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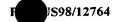
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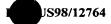
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ATCCTTCTGT	TAAAAATTT	CAGTTTATCA	ATTTGGTATT	TACTTTTTT	AAAGAGGCTG	562800
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CAATTGCCTT	TAAAACCCCT	TTTCCCATAT	ATACAGACTT	ATCACCATCT	CTAAGCTCAA	565500
CAGCCTCGTT	AATTCCTGTT	GATGCACCTG	ATGGTACGGC	AGCTCTTCCG	TAAGTTCCAT	565560

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567360

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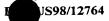
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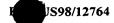
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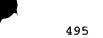


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